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VOL. 21 JANUARY, 1921 No. 1

THE FOOD REQUIREMENTS OF CHILDREN

I. TOTAL CALORIC REQUIREMENTS *

L. EMMETT HOLT, M.D., and HELEN L. FALES

NEW YORK

In the course of our metabolism observations on young children many interesting facts have been brought out with respect to the general food requirements as to total calories, distribution of the calories as fat, carbohydrate and protein, and other factors in the diet which must be considered. One notes in the literature on the food requirements of growing children a great difference of opinion among the various observers who have studied the subject. Many writers have taken up this problem from only a single point of view, such as the total caloric requirement, or the basal requirement, or the food needs in respect to one or another of the accessory food substances, the so-called "vitamins."

We have, therefore, thought it desirable to consider in its different aspects the whole subject of the food requirements of the child during the entire period of growth.

We shall discuss in this paper the total caloric requirements of children and the different factors which must be reckoned with in estimating the total calories. In succeeding papers we shall take up the proper distribution of the calories of the food as fat, carbohydrate and protein, also other important factors in the diet such as roughage, the difference in growth-promoting properties of the different proteins, the supply of essential inorganic salts and the accessory food substances or vitamins.

At various times and by various authors each of the different factors mentioned has been discussed, but as yet no one has attempted to correlate them all and study the food needs of the child in the entire aspect. The estimates of total caloric requirements of children made by some authors have been purely hypothetical, while others have been based on the requirements of adults.

Observations made during the last few years, especially in this country, have thrown new light on the question of the total calories

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needed by the growing child. It is essential to review not only this published work, but also most of the older observations, made chiefly in Germany. From these older observations conclusions have been drawn which do not seem to be warranted either by the number of children studied or the conditions under which they lived. For instance, one author made but a single observation on one child; another's observations were made almost entirely on his own children; those of a third were made on a considerable group of young children who were inmates of an orphan asylum, most of whom were very much under weight; a fourth studied three girls, two of whom were very much over weight.

It is recognized by all who have studied this subject that even in normal healthy children there are very considerable individual variations in food requirements. These variations are certainly much greater in abnormal children or in those studied under unusual conditions. Yet the small number of observations made by some of the German authors referred to are quoted over and over again in textbooks and periodical literature and have been made the basis of very broad and widely accepted deductions. In the light of more recent studies made on a larger scale, some of these deductions seem to be erroneous and misleading.

COMPONENT FACTORS OF CALORIC REQUIREMENTS

In calculating the total caloric requirement of a child there must be taken into account (1) the basal requirement, (2) growth needs, (3) needs for muscular activity, and (4) the food values lost in the excreta. The first of these, the basal requirement, is fairly uniform for children of the same weight. Growth requirements diminish rapidly from birth to the end of the third year and vary but little from this time until the tenth or eleventh year, after which they undergo a marked increase, which is maintained until growth is practically complete. The variation of this growth rate is fairly uniform with all children. Muscular activity, however, varies enormously with different children, but in general tends to increase steadily from birth to puberty. The caloric value of the foodstuff lost in the excreta is subject to very little variation in healthy children of the same age, unless there are marked differences in the diets.

Basal Requirements.—A great deal of accurate information has been accumulated regarding basal requirements, that is, the needs of the body at complete rest. This knowledge has been obtained by calorimetric observations made by Benedict and Talbot, DuBois, Murlin and others in this country and by Voit and Pettenkoffer, Rubner and Heubner, Schlossman and Murschhauser, and Magnus-Levy and others abroad. Some have based their comparison of individuals on the

body surface, but the body weight has been most frequently employed. Many studies have been made of the basal metabolism of adults, both in health and disease, and a large number of observations have been made on infants, especially the new-born. The intervening period, from the age of one year until the end of puberty, has not been so generally investigated. Talbot and Benedict are the only observers who have studied this entire period systematically.

Benedict [1] has recently presented the results of about 250 observations made by himself and Talbot on children of both sexes, more than half of whom were over one year of age. The range of individual

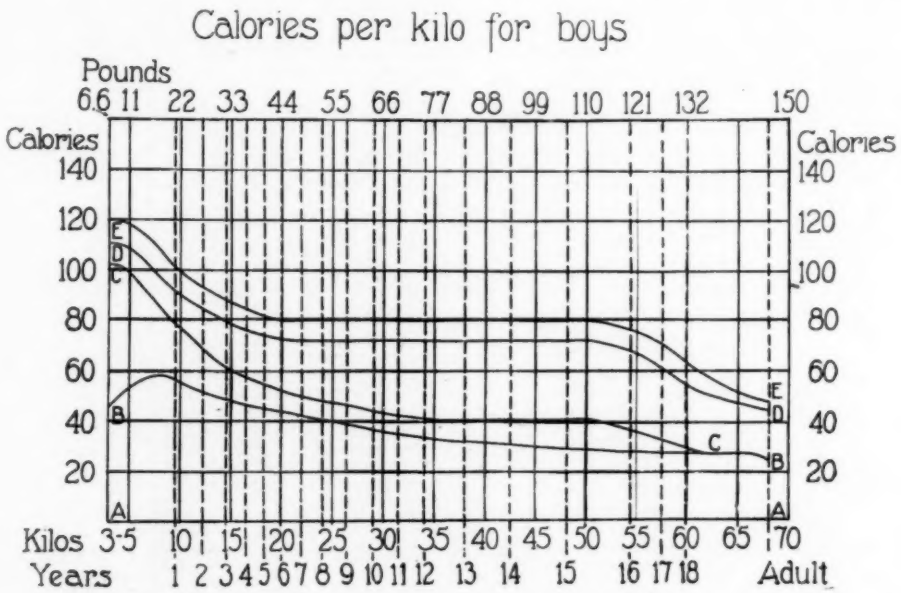

Fig. 1.—The solid vertical lines indicate weights in kilos; the broken lines, approximate weights at each year of age. The space between lines AA and BB shows allowance for basal metabolism; between BB and CC, that for growth; between CC and DD, that for muscular activity; between DD and EE, food values lost in excreta. The space between the lines AA and EE shows the total caloric allowance per kilo.

variation in the values obtained was considerable, but the number of observations made is so large that the data seems sufficient to warrant us in accepting their curves as representing the average for the period of growth.[2] They have shown that the basal metabolism per

1. Benedict, F. G.: Boston M. & S. J. **181**:107 (July 31) 1919.

2. In a personal communication Talbot stated that the curve for the latter years of childhood may need some revision, since up to the present time the number of observations has not been sufficient to establish definitely this part of the curve.

kilo of body weight is at birth "specifically low," that it rises rapidly until the body weight has reached seven to nine kilos and then diminishes slowly to adult life (Charts 1 and 2). There is some difference between the basal needs of boys and girls. After a weight of ten kilos (about one year) is reached the basal requirement of boys exceeds that of girls until a weight of about thirty-five kilos is reached (at about 11 years of age), when the basal needs of girls for a time exceed those of boys. Benedict and Talbot found that the basal caloric requirement increases with age but the relationship is best expressed as calories per unit of body weight or of body surface. There was, in their opin-

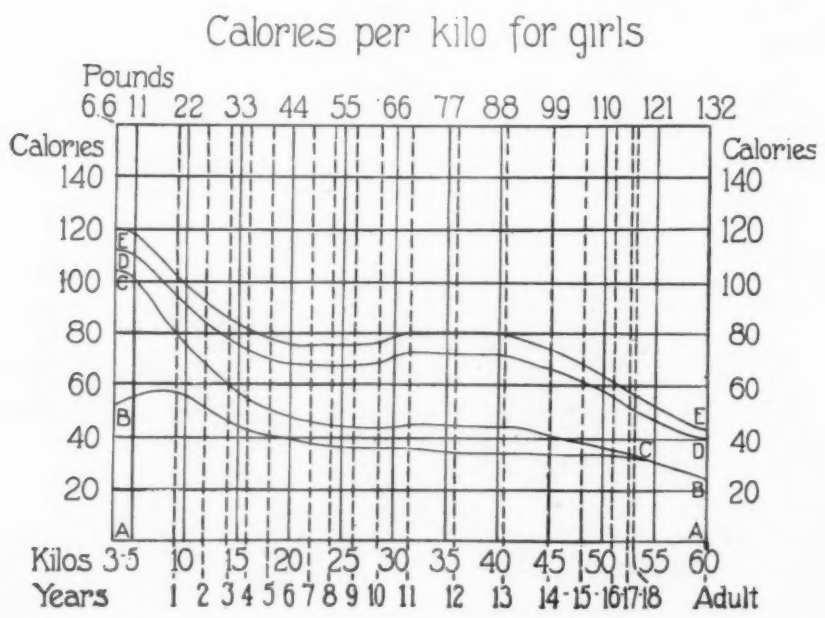

Fig. 2.—The vertical and curved lines have the same significance as in Chart 1.

ion, no closer consistency in the caloric values when expressed per unit of body surface than when expressed per unit of body weight. In our discussion, therefore, we shall use the more convenient standard—the unit of the body weight.

Magnus-Levy [3] in 1899 studied the basal metabolism of twenty-five children of 2 years of age and upward, but the ages studied were widely scattered and the values obtained for different individuals show wide variation. For the most part his values are higher than those obtained by Benedict and Talbot.

3. Magnus-Levy and Falk: Arch. f. Anat. u. Physiol., 1899, p. 314.

DuBois [4] made studies of the basal metabolism of eight boys between 12 and 14 years of age. The values he obtained are also somewhat higher than those of Benedict and Talbot, but are lower than those of Magnus-Levy. Two years later he [5] studied the same boys and found that the basal metabolism per kilo had diminished but that the values obtained fell on the curve which he had deduced, using his own observations and those of others. The reduction in basal calories per kilo in case of these boys was only the normal reduction which takes place steadily with increasing years.

On the whole, it seems reasonable to accept the values for basal requirement given by Benedict and Talbot as representing what they have termed "the irreducible minimum" which must be supplied to the human organism for maintenance.

Growth Requirements.—We shall not at this point consider the special growth needs, such as necessary vitamins or the need of supplying proteins which have the essential amino-acids, but only the energy requirements for growth which are met by the fat, carbohydrate and protein furnished in the ordinary articles of food. The caloric requirements for growth must, it is obvious, be greatest when growth is most rapid and diminish at the period when growth is slower. The rate of growth is most rapid during the first year of life, diminishing greatly in the second year. It is again accelerated at the approach of puberty. The diminution in the growth rate during the early years and the acceleration during the later years is indicated by the annual increase in weight and height from birth up to the time when the body is completely grown. This average increase is shown for both sexes in Chart 3. If we combine the curve representing the annual increase in weight and that for the annual increase in height we obtain a curve which may be taken to represent the annual increase in the size of the body during the period of growth. This rate of increase steadily increases in both sexes after the age of 10. In boys by the sixteenth year and in girls by the thirteenth year it is nearly twice as great as it is at ten years.

In calculating the total caloric requirements in the past it appears that sufficient consideration has not been given to these variations in the rate of growth. The increase in the body's needs for growth is not uniform as age advances from early childhood through the period of adolescence.

Using as a basis for calculation the annual increase in weight, it is possible to estimate very approximately the number of calories needed

4. Dubois, E. F.: Arch. Int. Med. **17**:887 (June) 1916.
5. Olmstead, W. H., Barr, D. P., and DuBois, E. F.: Arch. Int. Med. **21**:5 (Jan.) 1918.

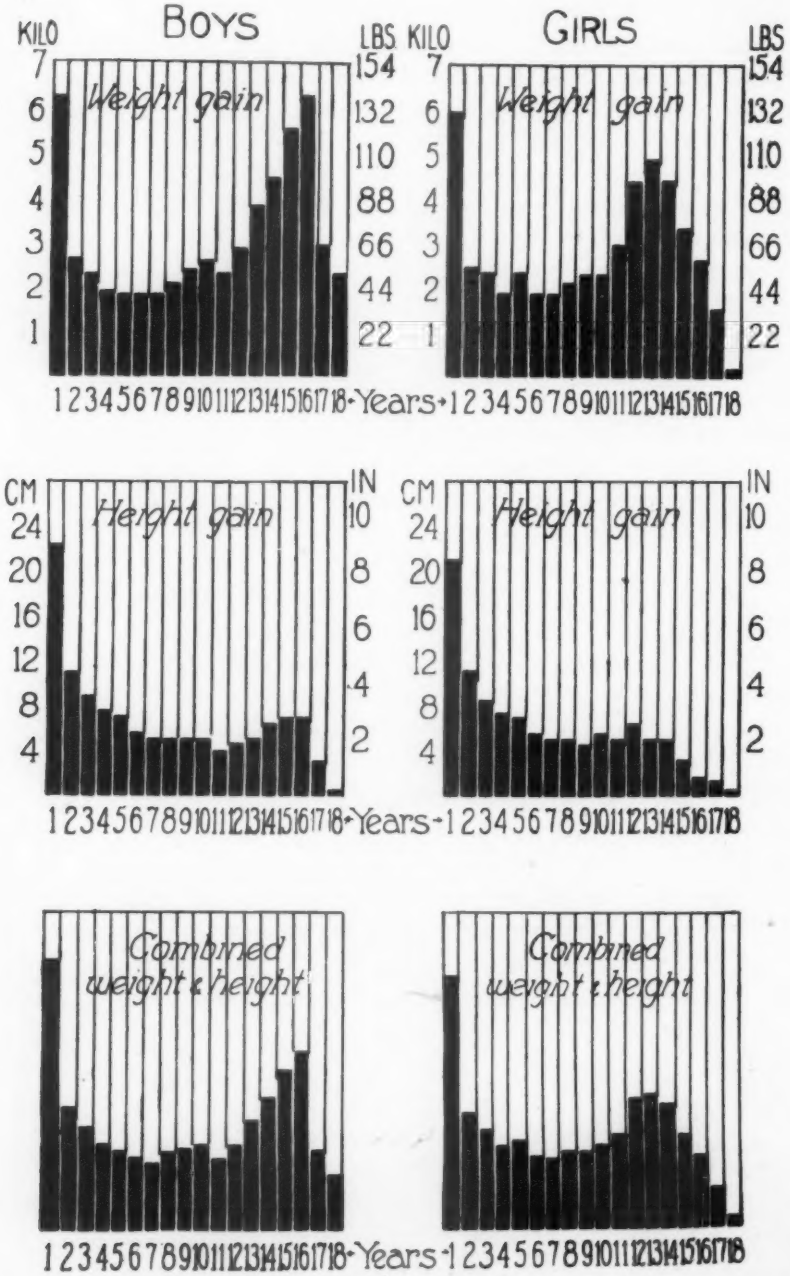

Fig. 3.—The heavy black verticals of the two upper charts show the annual gain in weight in kilos and pounds, and the gain in height in centimeters and inches, for both sexes. The lowest charts show values obtained by combining the two.

for growth by a child at any given age and weight. Rubner [6] estimates that about 80 calories per diem are needed to increase the weight of the human body one kilo in one year. This value multiplied by the average increase in kilos per annum would give approximately the number of calories needed daily for growth. On this basis the daily caloric need for normal growth for boys is over 200 calories during the second year; between 4 and 8 years it diminishes to about 150 calories, then rises steadily, reaching over 500 calories daily during the sixteenth year, after which it rapidly falls (Chart 5).

Requirements for Muscular Activity.—It is difficult to estimate with even approximate accuracy exactly how many calories should be allowed for muscular activity. Allowance must be made for all activity, whether productive or unproductive. Even the energy expended in the process of digestion must be taken into account in estimating these needs. Benedict states that the energy needed to digest the food taken uses up about 6 per cent. of the total calories of the diet. This he terms the "cost of digestion." It is a factor not usually considered but is important. Like the food value lost in the excreta it is one of the inevitable losses and one for which allowance must be made in estimating the total caloric requirement.

The requirements of individual children for activity differ very greatly, more widely than they do in any other respect. A nervous, lively, energetic child will certainly use up more calories in activity than one of quiet, placid temperament and indolent muscular habits. How much the difference is between the actual needs of these two types we can, with our present knowledge, only conjecture.

Lusk [7] has estimated that during the period from four to fifteen years the very active child requires a little more than double the total calories of a quiet child. Since three of the four factors which make up the total calories, namely, basal requirement, growth requirement and the food value lost in the excreta, are nearly the same for these two types of children, it would appear that practically all of the increased allowance which Lusk proposes, or considerably more than half the total food taken, is used up by the very active child in muscular activity. For young children this seems excessive. It certainly cannot be taken as an average. At any age it is probably applicable only to a small group.

Lusk allows for the child of moderate activity about one-third more calories than for the quiet child. This value is probably more nearly correct for the younger children, but the allowance is not enough for boys after 12 years of age and probably not for girls.

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6. Rubner, M.: Das Problem der Lebensdauer und seiner Beziehung zu Wachstum und Ernährung, 1908.

7. Lusk, G.: J. A. M. A. **70**:821 (March 23) 1918.

A steady increase in the calories which are needed for activity must be allowed as age advances. As soon as a child learns to run about a great increase in activity takes place, and with the normal healthy child activity steadily increases with each year of life, at least up to the period of adolescence.

DuBois estimates that walking at a moderate pace on the level uses three times the basal requirement. On this basis, a boy of about 30 kilos weight, that is, of about 10 years of age, walking on the level for two hours, would require an increase of 270 calories to supply energy for this activity.

The great difference in food requirements of children because of the difference in their activity is not in most cases sufficiently taken into account. If the increased caloric need of the active child is not supplied by the diet, growth inevitably suffers and, as Talbot [8] has pointed out with respect to infants, there is no gain in weight. The same consequence—failure to gain weight——follows when for any reason the digestive organs are not equal to the extra task imposed by increased ingestion of food. All these factors, and not simply the average needs as worked out for large groups, must therefore be taken into account when one is considering the needs of a single child or a small group.

Food Values Lost in the Excreta.—No accurate observations on this point have been published regarding children over 6 years of age. Our own studies lead us to the opinion that this factor varies less with age than do the other three factors which make up the total food requirement, and that in health a loss of calories equal to about 10 per cent. of the food intake is approximately correct for children of all ages. Some variation in children of the same age and weight will of course be seen, depending upon the amount and nature of the food, the care of preparation, on thoroughness of mastication, etc.

Extensive work done by the Department of Agriculture on the diet of adults has established quite definitely that the loss in the excreta, when a mixed diet is taken, averages about 9 per cent. of the total calories ingested. Benedict states that when a mixed diet is properly balanced and the digestion is normal, the loss in the excreta does not average more than 6 per cent. Atwater and Sherman, who followed the metabolism of three six-day bicycle riders, found an average loss in the excreta of nine per cent. of the total calories taken.

Müller [9] made a careful study of the diets of thirty-two children from 2 to 6 years of age. In order to determine the exact food value lost in the excreta, he dried the feces and urine of each child, as well

8. Talbot, F. B.: Am. J. Dis. Child. **18**:4 (July) 1919.
9. Müller, E.: Biochem. Ztschr. **5**:143, 1907.

as a sample of the composite food of each, and determined the exact caloric value of these substances by burning samples in a bomb calorimiter. The average caloric value of the dried feces was 5.0 calories for each gram of dried matter, the range being from 4.6 to 5.4 calories per gram. The urine showed a caloric value ranging from 8.7 to 13.9 calories for every gram of nitrogen which it contained, the average being 10.4 calories per gram of nitrogen. The average daily caloric loss in the feces of the children observed by Müller was 5.9 calories per kilo of body weight. The average loss in the urine was 4.6 calories per kilo of body weight. This gave an average total daily loss in the excreta of 10.5 calories per kilo. The average intake being 103.7 calories per kilo, the average loss in the excreta was, therefore, 10.1 per cent. of the intake. The individual loss ranged from 8 to 14 per cent. of the total caloric intake.

In our own observations we have found that healthy children under 6 years of age taking a mixed diet have from 10 to 20 gm. of dried matter in the daily stools. This represents a loss in the stools of from 50 to 100 calories, using as a basis for calculation Müller's average figure for the caloric value of dried feces. According to our observations, which confirm those of other authors, children from 1 to 6 years of age taking a mixed diet excrete from 4 to 6 gm. of nitrogen in the urine daily. Using Müller's average figure for the caloric value of urine, this indicates a loss of from 40 to 65 calories daily. The combined loss in urine and feces by children from 1 to 6 years of age is, therefore, from 90 to 165 calories daily. This is approximately 10 per cent. of the calories usually given at these ages, and, therefore, corresponds closely with the value suggested by Talbot for infants.

Using Müller's average caloric values for feces and urine, we have calculated the exact caloric loss through the excreta in five observations on normal children. The loss was found to range in these cases from 8.8 to 10.6 per cent. of the total calories of the food taken and the average was 9.6 per cent. We found that children suffering from a mild form of chronic intestinal indigestion had a loss through the excreta ranging from 10 to 15 per cent. of the total calories taken, while in cases of severe chronic intestinal indigestion the loss was at times as high as 25 per cent. of the total calories of the food taken. A summary of these findings is shown in Table 1.

In cases of severe chronic intestinal indigestion the total food value lost in the stools must frequently be much greater than the 25 per cent. estimated. For in such cases there is usually a very large loss of carbohydrate through fermentation in the intestine. The chief products of this fermentation—gases and volatile fatty acids—do not appear in the dried matter of the stool and we have no convenient method of

estimating them. Moreover, there is often some loss of protein due to putrefaction, which is represented in the stool mainly by volatile substances. How many calories these additional losses represent it is difficult to estimate.

TABLE 1.—AVERAGE NUTRITIVE VALUES LOST IN EXCRETA

Condition of Children	Number of Observations	Age in Years	Dried Weight of Feces, Gm. Daily	Calories Lost in Feces	Nitrogen in Urine, Gm. Daily	Calories Lost in Urine	Total Calories Lost in Excreta	Calories in Food Taken	Per Cent. of Calories in Excreta	
									Aver.	Range
Normal.....	5	2-3.5	11.6	58	5.3	55	113	1,177	9.6	8.8-10.5
With mild chronic indigestion.....	10	1-3	14.5	73	4.9	51	124	1,008	12.3	10.0-14.5
With severe chronic indigestion.....	12	2.5-9*	21.1	106	5.8	60	166	865	19.2	12.9-24.7

* Some of the children in this group, although older, were much undersize and underweight and were therefore comparable to those in the other groups.

On the whole, our estimate of 10 per cent. of the calories for loss in the excreta seems a reasonable average allowance for normal children taking a mixed diet. This allowance would certainly be high for nursing infants, however, since our observations have shown that these infants utilize from 95 to 99 per cent. of the fat intake and a very much higher proportion of the protein intake than do artificially fed infants.

TOTAL CALORIES

A number of authors have made observations on individual children or groups of children to determine the total calories taken at different ages. A comprehensive survey of the literature on this subject up to 1917 has been made by Lucy H. Gillett.[10] In her report is given an extensive bibliography and a summary of such values reported by various authors as have been based on actual observations of food taken. Such observations are surprisingly few. Most of them have been made by the German authors and have been so widely quoted and have formed the basis of so many calculations for total calories per kilo that it seems worth while to go into detail regarding the children studied. There are objections to using the results obtained with almost all the small groups observed for the determination of the requirements of average healthy children living under normal conditions.

Hasse[11] calculated the calories taken by six girls belonging to well-to-do families. The ages of these children ranged from 2 to 11 years. All were in good health, but, as compared with our standards

10. Gillett, L. H.: Publication 115, N. Y. Assn. for Imp. of the Cond. Poor, 1917.

11. Hasse, S.: Ztschr. f. Biol. **18**:553, 1882.

two were under weight, while the others were somewhat over weight. The two under-weight children, who were 2 and 5 years of age, took respectively 102 and 90 calories per kilo, rather high values for their ages. The children of 3 and 3½ years took 77 and 81 calories per kilo, about the usual for their ages. The two older girls, 9 and 11 years of age, took only 65 and 61 calories per kilo, respectively, but these girls were considerably over average weight.

Herbst [12] also observed six children in well-to-do families. Three were boys, aged 2, 4 and 10 years. The youngest was considerably over weight, the other two practically the average weight for their ages. They took respectively 90, 87 and 66 calories per kilo. The other three children were girls in their eleventh, thirteenth and fifteenth years. The first two were very much over weight, the third somewhat over weight. They took respectively 45, 41 and 38 calories per kilo. These values are very low indeed, but the children observed were in a rather exceptional physical condition and data derived from the study of their food can hardly be used as a basis for estimating the needs of the average child. These observations, however, confirm the generally accepted opinion that the food requirements per kilo of overweight children are much lower than those of children of average weight for their age.

Müller [9] studied twenty-three boys and nine girls, each for a six-day period, and collected and analyzed the urine and feces of each child, as well as recording the exact amount and kind of food taken. The ages of the children ranged from 2 to 6 years. The children were reported to be healthy and free from nutritional disturbances, but all were inmates of an orphan asylum and appear to have been fair examples of what is commonly spoken of as "institution children." Nearly all of the children were under weight, the boys almost without exception markedly so. As might have been expected with children of this class, the intake per kilo was high, the average for the group being 104 calories per kilo. Two-thirds of the boys weighed between 11 and 15 kilos and these boys, all under weight, took on the average 113 calories per kilo. One boy of 4 years with the weight (12.6 kilos) of an average child of about 2 years, took 132 calories per kilo; another child, 6 years old, of about the same weight as the one just mentioned, took 126 calories per kilo.

The girls, who were not so much under weight as the boys, took on the average about 15 calories per kilo less than did the boys. These values correspond fairly well with the usually accepted ones for their ages, except in the single instance of one girl who was about the average weight for her age and who took only 71 calories per kilo.

12. Herbst, O.: Jahrb. f. Kinderh. **46**:322, 1898.

Müller's observations were made in winter. He thinks that season should be taken into account in estimating the food needs. His results show that children who are much below normal weight require much more food per kilo than do normal children. All the facts concerning the children observed must be known in order to appreciate and properly interpret the data obtained. We are no more justified in basing our estimates for normal requirements upon the results obtained with these underweight children than on the results with Herbst's overweight girls.

Uffelmann [13] made observations on his own children, all boys, at the age of 2, 4, 10 and 15 years. The oldest and youngest were somewhat, the other two very much under weight. Contrary to general experience, the calories per kilo reported to be taken by these children were low. We can hardly resist the inference that, if the diet at the time of observation was typical of that usually taken, these children were below weight because underfed.

Camerer [14] made extensive observations of the amount of food taken by his own children, four girls and one boy, at different times extending over a period of years. In the observations made at ages under 7 years the calories per kilo taken by both sexes were about the usual for those ages. In the later observations, however, the calories per kilo were very low and diminished rapidly with increasing age, so that in the observations made at ages over 15 years the calories per kilo taken by both sexes were only a little above the basal requirements as determined by Benedict and Talbot. Camerer's girls were on the average much below the average weight for age at the time of observation and during the early years the boy was somewhat under weight. Accordingly a high caloric intake would have been expected. The fact that, on the contrary, the calories per kilo taken by these children were very low suggests, as we have said in regard to Uffelmann's children, that the under weight was possibly due to under feeding.

Baginsky [15] has given values obtained from a study of a number of children convalescent from various forms of acute disease and with one exception much under weight. As might be anticipated, his values are for the most part high.

E. H. Starling,[16] quotes Carl Tigerstedt, who made forty-seven observations on children ranging from 4 to 14 years of age. The weights unfortunately are not given, only the calories per kilo. The striking thing in these observations is the wide range of calories taken.

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13. Uffelmann, J.: Hygiene des Kindes, 1881.
14. Camerer: Stoffwechsel des Kindes, 1896.
15. Baginsky, A.: Arch. f. Kinderh. **23**:119, 1897, and **16**:398, 1893.
16. Starling, E. H.: The Feeding of Nations, 1919.

For example, in four observations on children in their fifth year the range was from 73 to 114 kilos; in five observations for the seventh year, from 71 to 102; nine observations for the twelfth year, from 44 to 89; seven observations for the fourteenth year, from 43 to 82 calories per kilo. Starling calls attention to the dangers involved in basing estimates for food requirements on averages, especially when these include only a small number of observations.

In marked contrast to the values found by most of the authors mentioned above are those of Gephart,[17] whose observations were made in quite a different manner. His method was that employed by other writers in studying the actual amount of food consumed by soldiers in camps, and seems to be a reliable way of determining the average number of calories taken. Gephart studied the diet of about 350 boys in a large boarding school (St. Paul's, Concord, N. H). in the following manner: He first calculated the caloric value of the entire amount of food purchased during the period of observation, the entire school year. From this he subtracted the values obtained by analyzing at various times the garbage and the waste. The remainder he divided by the total number of meals served, and thus obtained an average caloric value per meal for the school. In addition to the meals which were provided by the school, the boys were accustomed to buy from a confectioner's shop considerable extra nourishment—sweets, chocolate, cakes, etc. The total amount purchased during the period was known and was apportioned by Gephart among the boys of the whole school. The calories furnished by this additional food were found to be about one-eighth of the total daily consumption.

TABLE 2.—SUMMARY OF GEPHART'S OBSERVATIONS ON BOYS AT ST. PAUL'S SCHOOL

School	Average Age in Years	Average Weight		Average Calories per Kilo			Average Total Daily Calories
		Kilos	Pounds	School	Food Shop	Total	
Lower	13.5	43.6	96	98	15	113	4,949
Middle	14.5	50.8	112	88	13	101	5,126
Upper	16.1	60.6	133	71	11	82	4,997

The average daily caloric intake was found to be about 5,000 calories per boy, and all but the group of the oldest boys took over 100 calories per kilo. The boys were divided into three groups, the lower, the middle and the upper school. In Table 2 are given the ages, average net weight, calories per kilo furnished by the school, additional calories purchased at the confectioner's, average total calories per kilo and average daily total calories for each group.

17. Gephart, F. C.: Boston M. & S. J. **176**:17, 1917.

While the conclusions which might be drawn from these observations may perhaps be open to question, still, the results show what amount of food is actually taken by the average American school boy at the ages studied, under the special conditions represented by these observations. It may be argued that these conditions were not average but somewhat exceptional. The boys were living in a rigorous climate; they were taking a great deal of active out-of-door exercise and they were at an age when growth is most rapid. Furthermore, the well-known disposition of boys of these ages to stuff themselves with food apparently beyond their actual needs must also be taken into account. Still when due allowance has been made for all these conditions, the fact remains that the enormous appetite of active, growing boys represents a physiological need which in the past has not been given sufficient consideration.

Studies made on such large groups are likely to give results much nearer the truth than observations made on a few individuals or the children of one family, no matter how carefully these observations have been made. The results of the German observations which we have quoted would lead one to allow too little food for children during the active growing period.

The Department of Agriculture has made many observations on the amount of food taken by families, including children, but has not determined experimentally what proportion of the food was taken by each child. They have apportioned the diets theoretically according to a commonly used system of coefficients; for example, assuming that if a man takes one portion, a woman takes 0.8, a boy of 12 takes 0.8, a boy of 8 takes 0.7, etc.

Schedules Proposed by Various Authors.—Several authors have proposed complete schedules of theoretic caloric requirements from infancy to adult life. These have been based either on their own observations or on those of others. Most of these observations we have just discussed.

Among the German observers, Camerer's schedule has been most often quoted as a standard. His suggested allowance for boys is 89 calories per kilo at the age of one year and diminishes to 75 calories at 4 years. For the age of 5 years the allowance is increased to 84 calories. From that age the allowance decreases rapidly and steadily to adult life. His values after 6 years are low, and after 9 years extremely so. After the twelfth year his allowance is but little above the basal requirements as shown by Benedict and Talbot.

Steffen [18] offers a schedule for children up to six years of age and allows over 100 calories per kilo through this entire period.

18. Steffen, W.: Jahrb. f. Kinderh. **46**:332, 1898.

Uffelmann has proposed a schedule for the first five years of life. His values are rather low, ranging from 88 calories per kilo at one year to 68 calories at five years.

Gillett and Sherman, after giving due consideration to the observations which have been published and which are summarized by Gillett, present a table of suggested values for total daily calories for children of both sexes throughout the entire period of growth. They allow a considerable range of variation. Their allowance diminishes gradually to 68 calories per kilo at 9 years and is maintained at that figure up to the age of 13, dropping to 65 at 14 years. After this age the average allowance is rapidly decreased to 55 calories per kilo at 16 years. This decrease in calories per kilo during the period of most rapid growth after the age of 13 seems to us injudicious.

Lusk has recently published estimates for total calories. As already mentioned, he makes a very large allowance for activity and gives three curves—for the quiet child, the active child and the very active child. He allows the same percentage increase in total calories for increased activity, quite irrespective of age and weight. That is, his values for the active child are about one and one-third times those for the quiet child at all ages, while the values for the very active child are about twice those for the quiet child at all ages. Accordingly, his estimates for total calories for the very active child and even for the child of moderate activity, are extraordinarily high for the early years, for example, 193 and 129 calories per kilo, respectively, for a boy of 2 years. The diminution in calories per kilo with increasing years is rapid according to all three of his curves. His values for the quiet child after the age of 13 are very little above the calories necessary for basal metabolism and for normal growth. No allowance is left for activity, which of course can never be reduced to zero.

Gillett and Sherman and also Camerer give schedules for girls as well as for boys. According to both the allowance for girls is considerably lower than that for boys, and from the twelfth year the allowance exceeds only by very little the needs for basal metabolism and growth.

PROPOSED SCHEDULES FOR CALORIES PER KILO

In the light of our own observations and those of others, the theoretical schedules for calories per kilo of body weight shown in Charts 1 and 2 and Tables 3 and 4 are suggested. The charts show the curves and the tables the actual figures, on which the curves are based, for the different factors which make up the total calories per kilo. The tables show also the percentage allowance for each of the different factors.

TABLE 3.—Suggested Calories per Kilo for Boys

Weight, Kilos	Calories per Kilo					Per Cent. of Calories for				Total Calories Daily
	Basal	Growth	Activity	Excreta	Total	Basal	Growth	Activity	Excreta	
3	46	56	8	10	120	38	47	7	8	360
4	50	52	8	10	120	42	43	7	8	480
5	54	46	8	10	118	46	39	7	8	590
6	56	38	10	10	114	49	33	9	9	685
7	57	32	11	10	110	52	29	10	9	770
8	56	28	12	10	106	53	26	11	10	850
9	55	25	12	10	102	54	24	12	10	920
10	54	22	13	10	99	55	22	13	10	990
11	53	19	14	10	96	55	20	15	10	1,060
12	52	16	16	9	93	56	17	17	10	1,120
13	51	14	17	9	91	56	16	18	10	1,180
14	50	13	17	9	89	56	15	19	10	1,240
15	49	12	17	9	87	56	14	20	10	1,300
16	48	10	18	9	85	56	12	22	10	1,360
17	47	9	19	8	83	56	11	23	10	1,410
18	46	8	20	8	82	56	10	24	10	1,470
19	45	7	21	8	81	56	9	25	10	1,540
20	44	7	21	8	80	55	9	26	10	1,600
22	42	7	23	8	80	53	9	28	10	1,760
24	41	8	23	8	80	51	10	29	10	1,920
26	39	8	25	8	80	49	8	31	10	2,080
28	38	7	27	8	80	47	9	34	10	2,240
30	36	7	29	8	80	45	9	36	10	2,400
33	35	7	30	8	80	44	9	37	10	2,640
36	33	8	31	8	80	41	10	39	10	2,880
39	32	9	31	8	80	40	11	39	10	3,120
42	31	10	31	8	80	39	12	39	10	3,360
45	30	11	31	8	80	38	13	39	10	3,600
48	30	11	31	8	80	38	13	39	10	3,840
51	29	11	31	8	79	38	13	39	10	4,030
54	29	8	31	8	76	38	11	41	10	4,100
57	28	5	30	7	70	40	7	43	11	3,990
60	27	2	27	7	62	43	3	44	10	3,720
66 (Adult)	25	0	18	5	48	52	0	38	10	3,265

TABLE 4.—Suggested Calories per Kilo for Girls

Weight, Kilos	Calories per Kilo					Per Cent. of Calories for				Total Calories Daily
	Basal	Growth	Activity	Excreta	Total	Basal	Growth	Activity	Excreta	
3	51	51	8	10	120	43	43	6	8	360
4	53	49	8	10	120	45	41	6	8	480
5	55	45	8	10	118	47	38	7	8	590
6	56	38	10	10	114	49	33	9	9	685
7	56	33	11	10	110	51	30	10	9	770
8	57	27	12	10	106	54	25	11	10	850
9	56	24	12	10	102	55	23	12	10	920
10	55	21	13	10	99	56	21	13	10	990
11	53	19	14	10	96	55	20	15	10	1,060
12	51	17	16	9	93	55	18	17	10	1,120
13	49	16	16	9	90	54	18	18	10	1,170
14	47	14	17	9	87	54	16	20	10	1,220
15	45	12	19	8	84	54	14	22	10	1,260
16	44	11	19	8	82	54	13	23	10	1,310
17	43	10	19	8	80	54	12	24	10	1,360
18	42	9	19	8	78	54	12	24	10	1,400
19	41	8	20	8	77	53	11	26	10	1,460
20	40	7	21	8	76	53	9	28	10	1,520
22	38	8	22	8	76	50	11	29	10	1,670
24	37	8	23	8	76	49	11	30	10	1,820
26	36	8	24	8	76	48	10	32	10	1,980
28	36	8	25	8	77	47	10	33	10	2,155
30	36	9	26	8	79	46	11	33	10	2,370
33	35	10	27	8	80	44	12	34	10	2,640
36	35	10	27	8	80	44	12	34	10	2,880
39	35	10	27	8	80	44	12	34	10	3,120
42	34	9	27	8	78	44	11	35	10	3,276
45	34	7	26	7	74	46	9	35	10	3,330
48	33	5	22	7	67	49	8	33	10	3,216
51	32	3	21	6	62	51	5	34	10	3,162
54	31	0	18	5	54	57	0	33	10	2,916
60 (Adult)	25	0	15	4	44	57	0	33	10	2,640

The basal requirement adopted is that of Benedict and Talbot. This, it will be seen, after reaching a maximum at about the ninth month, falls steadily through the entire period of growth to adult life. The basal requirement per kilo for girls is lower than that for boys up to the age of 11 years, after which it is higher than that for boys until the completion of growth.

The growth allowance has been calculated from the average normal rate of growth, which has been well established. The calories allowed for growth fall steadily from the first year to the sixth year, then remain practically constant up to eleven years for girls and thirteen years for boys, when a marked increase takes place. This increased need is evident for about three years with both sexes, after which the growth needs rapidly diminish to zero.

The needs for basal metabolism and for growth, though subject to considerable individual variation, are, as averages, practically irreducible.

The allowance for activity is admitted to be hypothetical. For reasons previously given, this has been increased steadily from the second to the thirteenth year for boys and to the twelfth year for girls. Whether the allowance for activity should be further increased during the period of most rapid growth (in girls from the twelfth to the fourteenth or fifteenth year and in boys from the thirteenth to the seventeenth) is somewhat doubtful. It is a matter of common observation that while the body is increasing so rapidly in size as it does at this time, "the lazy age," there is frequently seen in both sexes a growing disinclination to active muscular exertion, which is usually accompanied by a corresponding disinclination to mental activity, sometimes amounting almost to mental lethargy. A very considerable stimulus may be needed to voluntary effort, both mental and physical. This is not surprising; it is rather to be expected and may be considered physiologic. The opinion is not only an impression from our own observations but is confirmed by the head masters and athletic directors of six large schools for boys with whom we have discussed the question. For the reasons above given we have felt that no increase in the caloric allowance per kilo for activity should be made during these years of most active growth; possibly even a slight reduction should be considered.

The number of calories we have allowed for loss in the excreta is 10 per cent. of the total after the first year of life, during which period a somewhat smaller proportion should be allowed, certainly for nursing infants.

With the values proposed for the different factors just discussed the total calories per kilo are for both sexes about 120 during the

early part of the first year, diminishing to 100 at one year, and reaching 93 calories per kilo at 2 years. After the second year there is an appreciable difference between the total calories per kilo allowed for boys and for girls, owing largely to the difference in their basal requirement, that of girls being, from this time until the end of the tenth year, several calories lower than that of boys. The calories per kilo allowed for both sexes slowly fall, largely because of the slowing up of the growth rate. We have estimated that at 6 years the total for boys should be 80 calories per kilo and for girls 76 calories per kilo. This value we have continued for boys up to about the sixteenth year. For girls the calories per kilo have been increased from 76 to 80 during the eleventh year, since there is at this time an increased growth need and since the basal needs for this and the next few years are nearly uniform. This higher value is continued for girls to about the fourteenth year. After the sixteenth year in boys and the fourteenth year in girls, since there is a rapid decline in growth needs and possibly some reduction in activity, the total calories per kilo have been rapidly reduced to adult standard—about 48 for males and 44 for females.

The chief difference between our schedule for total calories per kilo and others which have been proposed, is that in our schedule the total calories per kilo are nearly uniform from the age of six to the end of the period of rapid growth.

In the practical application of these suggested values it must be borne in mind that each component part of the caloric requirement is subject to considerable individual variation. The curve suggested aims only to give averages. The calories actually given must vary to fit the individual needs. Activity is of course the most obvious variant. An extremely active child will undoubtedly utilize more calories than the average which we have allowed, while the needs of a quiet child may be supplied by somewhat less than our suggested values.

Another cause for variation in the caloric requirement for the individual is the relation of weight to height and age. Our observations and those of others show that the underweight child will take and utilize more calories per kilo than the child of average weight; while, as might be expected, one who is overweight does not take and does not need the average number of calories per kilo. The fact must be taken into account in making the caloric allowance for an individual child.

It seems reasonable to allow for the younger children a normal range of five calories per kilo above and below the average given, and to allow the older children a range of eight to ten calories above and below the average. For instance, the normal range allowed for a

boy of 2 years might be from 88 to 98 calories per kilo, for a boy of six from 72 to 88 calories and for one of 15 a range from 70 to 90 calories per kilo. When activity is excessive, however, an increase of 20 or even 30 calories above the average may be well utilized.

Comparison of Schedules Proposed.—In order to show the difference between our suggested schedule for calories per kilo and others which have been proposed, Table 5 and Chart 4 are given. The table shows the calories per kilo proposed by various authors for both boys and girls at different ages. This table brings out clearly the points already mentioned in discussing the schedules offered. The only schedule which allows more calories per kilo throughout the entire range of years than does ours is that of Lusk for the very active child. During the early years this schedule shows about twice as many calories per kilo as we have considered sufficient. The difference diminishes after the age of seven, until at the age of fifteen his values are but little above ours. Lusk's estimate for the child of moderate activity exceeds ours up to the age of twelve, after which his values fall considerably below ours. The other complete schedules, those of Gillett and Camerer, are much below ours after the age of seven or eight. The two schedules for girls show values very much below ours after the age of six years.

TABLE 5.—Comparison of Schedules for Total Calories per Kilo

Author	Age, Years															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Boys:																
Holt and Fales	100	93	88	84	82	80	80	80	80	80	80	80	80	80	80	75
Gillett	105	90	83	79	77	75	73	71	68	67	68	69	68	65	60	55
Lusk, quiet child	79	97	90	88	79	78	79	73	70	66	66	62	54	48	45	
Lusk, active child	...	129	117	116	105	105	105	97	93	88	83	82	73	66	62	
Lusk, very active child	...	198	177	175	158	158	159	146	139	132	124	123	109	98	93	
Camerer	89	80	78	75	84	77	72	67	63	58	55	52	49	47	45	42
Uffelmann	88	80	73	71	68											
Steffen	113	99	105	125	114	108										
Girls:																
Holt and Fales	101	94	87	82	78	76	76	76	76	77	80	80	79	74	67	62
Gillett	105	93	83	79	73	71	69	66	64	62	59	55	51	48	47	46
Camerer	89	80	78	75	70	67	64	62	60	58	55	51	47	43	41	39

On Chart 4 the basal metabolism and the growth needs are indicated by the heavily and lightly shaded areas respectively. As we have said, these are, as averages, practically irreducible. The various curves shown in the chart were obtained by plotting the values offered in the various schedules after subtracting the ten per cent. of the total calories which is lost in the excreta. Therefore, the space between the shaded areas and the various lines represents the allowance for activity according to the different authors. The great difference is at once apparent. The curves representing total calories per

kilo would be obtained by raising each of the curves shown by the addition to the values plotted of the ten per cent. allowance for loss in the excreta.

The curve based on Camerer's values shows very little allowance for activity except between the ages of 4 and 8 years and after the age of 13 years practically none at all.

The curve based on the average values offered by Gillett and Sherman does not differ greatly from our own up to the age of 7 years. From 7 to 14 years it is nearly parallel with ours, but somewhat

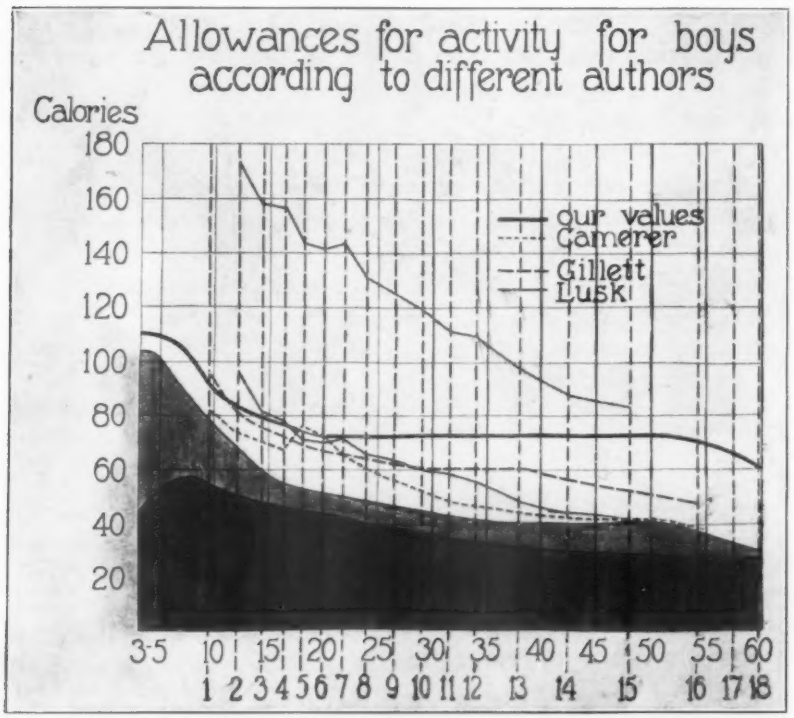

Fig. 4.—The heavily shaded area represents allowance in calories per kilo for basal metabolism; the lighter shaded area, the allowance for growth; both areas are according to our schedule. The spaces between the shaded areas and the lines above show what remains for activity according to the estimates of different authors. The solid vertical lines indicate weight; the broken lines, approximate weight at each year of age.

lower. After 14 years their curve falls rapidly. In our judgment they have allowed far too little for activity and growth during adolescence. As previously stated, they allow a fairly wide individual variation in total calories, but even if their maximum allowance is taken, the calories per kilo after the age of 14 are only about five

calories higher than the values shown on the chart, and therefore, still about fifteen calories per kilo lower than the values we have suggested.

The curve based on Lusk's values for the quiet child is almost identical with our own from 2 to 7 years. After this age his allowance for activity diminishes very rapidly and becomes practically zero at fourteen years. He gives a schedule, not represented here, for the child of moderate activity which, when plotted, is represented by a curve almost parallel to the one just discussed but about one-third higher. His curve for the very active child seems to give an extreme allowance for activity, certainly for the first ten or twelve years of life. At the age of 15 his allowance is not far above our own.

Total Daily Calories.—Charts 5 and 6 and Table 6 gives for boys and girls the average values for total daily calories based upon the values for calories per kilo just proposed by us. The curves shown on the chart are plotted on the basis of years of age, using the average normal weights at the different ages. The charts show not only the total daily calories but also the components—basal needs, growth needs, allowance for activity and for loss in the excreta—which together make up the total.

TABLE 6.—SUGGESTED TOTAL DAILY CALORIES

Age Years	Boys					Girls				
	Average Weight		Calories per		Total Daily Calories	Average Weight		Calories per		Total Daily Calories
	Kilos	Pounds	Kilo	Pound		Kilos	Pounds	Kilo	Pound	
1	9.5	22	100	45	950	9.3	21	101	45	940
2	12.2	27	93	42	1,135	11.8	26	94	43	1,110
3	14.5	32	88	40	1,275	14.1	31	87	40	1,230
4	16.4	36	84	38	1,380	15.9	35	82	37	1,300
5	18.2	40	82	37	1,490	18.2	40	78	36	1,410
6	20.0	44	80	36	1,600	20.0	44	76	34	1,520
7	21.8	48	80	36	1,745	21.8	48	76	34	1,660
8	24.0	53	80	36	1,920	23.9	53	76	34	1,815
9	26.4	58	80	36	2,110	26.2	58	76	34	1,990
10	29.1	64	80	36	2,330	28.5	63	77	35	2,195
11	31.4	69	80	36	2,510	31.5	69	80	36	2,520
12	34.2	75	80	36	2,735	35.8	79	80	36	2,864
13	38.0	84	80	36	3,040	40.6	89	79	36	3,210
14	42.5	94	80	36	3,400	45.0	99	74	34	3,330
15	48.2	106	80	36	3,855	48.3	106	67	30	3,235
16	54.5	120	75	34	4,090	51.0	112	62	28	3,160
17	57.5	127	69	31	3,945	52.6	116	58	26	3,060
18	59.8	132	62	28	3,730	52.8	117	56	25	2,950
Adult	68.0	150	48	22	3,265	60.0	132	44	20	2,640

The daily calories allowed for the boys and girls are about 950 at one year. They increase with succeeding years for both sexes, the increase for the boys being a little more rapid than for the girls until the age of 12 is reached. From 12 to 14 the total calories for the girls exceed those for boys. After fourteen, the allowance for boys is considerably greater than that for girls. The highest values for daily

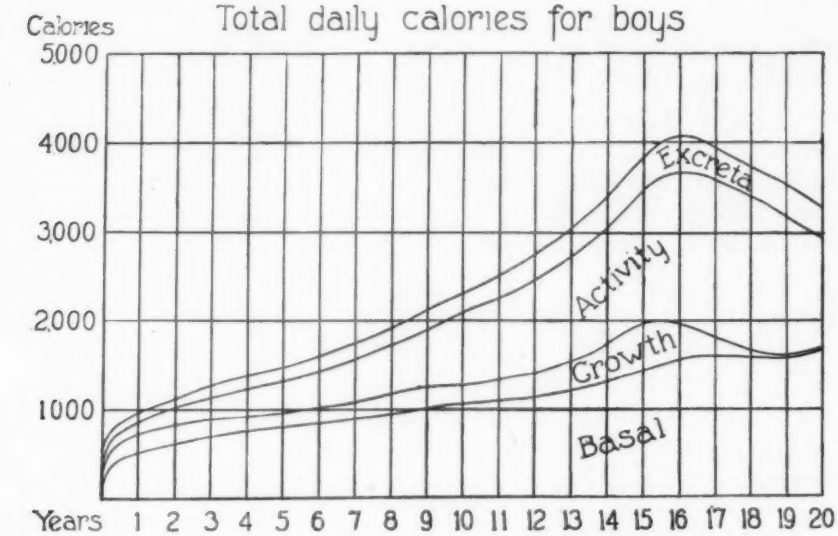

Fig. 5.—The distance between the base and the upper line shows the allowance for total daily calories according to age, from birth to adult life. The spaces between the various lines, from the base line upward, indicate the allowance for the different factors which make up the total, namely, for basal requirement, growth, activity and loss in excreta.

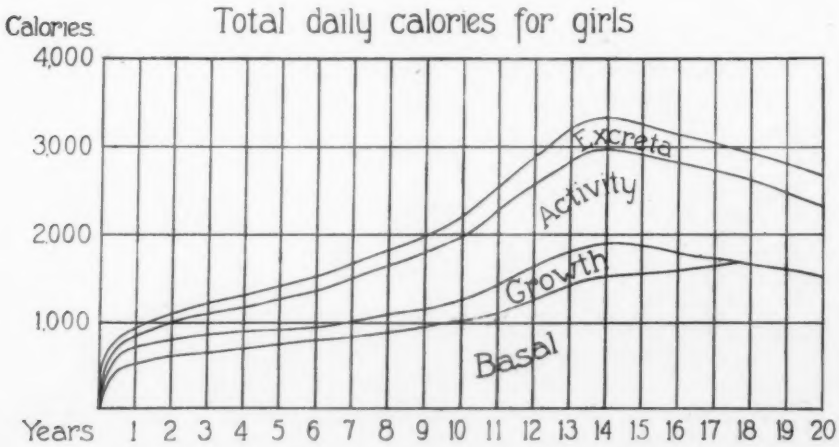

Fig. 6.—The curved lines and spaces have the same significance as in Chart 5.

calories are 3,330 for girls at the age of 14 and 4,100 for boys, at the age of 16. After these maximum figures are reached the values drop very rapidly to adult standards for moderate activity,—about 2,640 for women and 3,265 for men.

These charts show the provision for the increase in the growth needs during the period of adolescence. The growth need, calculated according to Rubner's formula, reaches for girls 380 calories daily during the thirteenth year, and for boys about 500 calories daily during the sixteenth year. It is this greatly increased need of calories for normal growth at this period that has not been sufficiently taken into account by many authors in estimating the total daily calories required by the growing child.

The large allowance for activity is of course the most debatable factor in our estimate. Some may think that this allowance is excessive but the more recent observations, particularly those of Gephart, seem to justify our position. Our values for the total daily caloric allowance for boys of the age of those studied by Gephart are still much below the calories which he found to be actually taken by the boys he observed. However, as we have stated, these boys were living under rather exceptional conditions and the calories taken by them can hardly be used as a basis for estimating normal averages.

According to our schedule the allowance for activity varies from 6 per cent. of the total calories during the first year to a maximum of 44 per cent. of the total calories during the period of adolescence. This does not seem excessive for this active period.

It is a common observation and an undoubtedly true one, that during adolescence the average boy or girl takes more food than the average adult man or woman. Unquestionably, this represents a real physiologic need. It is only by assuming such values for calories per kilo as we have proposed that one can reach a total daily caloric intake which will be in accord with these conditions.

The several authors who have given complete schedules for food requirements steadily increase the total daily calories with age through childhood and adolescence up to the standard allowance for adults. No one has up to the present proposed a schedule according to which the values for total daily calories exceed adult standards during adolescence and drop to adult standards with the completion of growth. This seems to us to be absolutely necessary. Unless this is done, the increasing growth needs must be deducted from the allowance for activity, leaving for the latter a very small remainder; or, on the other hand, if activity is maintained, growth must suffer. The modern child, boy or girl, is usually an active person during adolescence. If in school, he is required by school routine to take systematic exercise. If he has left school and entered industrial life he may be con-

tinually compelled to expend physical energy. In view of these facts it is evident that the food taken by perhaps the majority of boys of the poorer classes who are engaged in active industrial occupations during this period of rapid growth, is totally inadequate. An arrest of growth is the almost inevitable consequence of forced activity on a limited ration.

ORIGINAL OBSERVATIONS

Because there have been so few observations reported in the literature which give the calories taken by normal children under average conditions and because of the objections, already discussed, to drawing conclusions from a small number of observations, we have endeavored to collect a sufficient number of individual diet records to warrant some conclusions. This has proven to be a laborious and difficult task. We have at present, however, obtained dietary records from over one hundred selected children of both sexes from 1 to 16 years of age, who were healthy, well cared for, and normal as to digestion. They were almost all children in private families, living in excellent surroundings. The parents were intelligent people, interested in the purpose of our experiment, and willing to cooperate. The children were supposedly intelligently fed and it can be assumed that they were receiving diets fairly typical of those usually taken by well children.

A report of the net weight, height, activity, appetite, general condition, etc., was obtained, together with a record of the exact amount of each item of food taken by the child for four consecutive days. From these data the caloric value of the average daily diet was calculated. Not only was the value for the total calories obtained, but also the distribution of the calories as fat, carbohydrate and protein, which, together with other facts brought out, will be discussed in succeeding papers. Established caloric values of the common articles of food have been compiled in a convenient form by Locke.[19] These have been for the most part used. Other authors whose publications we have found valuable for reference in this study are Leach,[20] Sherman,[21] Lusk [22] and Jordan.[23] The values of a number of articles were calculated from the results of analyses made in our own laboratory.

This method of estimating the calories taken by children is of course not absolutely accurate but it undoubtedly gives a very close approximation. While there are slight variations from the usual caloric values of the food taken owing to differences in the methods of

19. Locke, E. A.: Food Values, 1917.
20. Leach, A. E.: Food Inspection and Analysis, 1920.
21. Sherman, H. C.: Chemistry of Food and Nutrition, 1919.
22. Lusk, G.: The Science of Nutrition, 1919.
23. Jordan, W. H.: The Principles of Human Nutrition, 1919.

preparing food, it is probable that these errors tend to balance each other and that the net result is approximately accurate. We feel certain that in no case did the child receive less food than was reported. It is not unlikely that in some cases a child actually took more food than was reported, especially the older children whose diet is not so carefully supervised and who are more likely to eat between meals without the knowledge of the parent. If there is, therefore, an appreciable error in the estimation of the calories, it is that the calculated amount is somewhat low.

The largest number of the records were of children under 11 years of age. There are from five to twelve observations for each year up to the age of 11. Beyond this age the number of observations for each year is too small to warrant definite conclusions.

In Chart 7 are shown the total calories taken by these children arranged according to age. The curves shown are those based upon the schedules proposed by us for average daily calories at different ages. The curve for boys is indicated by the solid line, that for girls by the broken line. The individual observations for boys are shown by the dots, those for girls by circles.

This chart shows, as was to be expected, a wide variation in individual observations. However, the observations mostly fall near the curves and up to the age of 11 the average would fall very near the curves. Beyond that age there are as yet too few observations to be conclusive. However, those made on older boys are very close to the proposed curve.

Some of the observations which vary most widely from the average curves deserve special mention. There were eight children in the series whose total calories taken amounted to over one-third more than the theoretical average requirement, but every one of these children was reported to be exceedingly active. There were only two children, both girls, whose total calories were more than one-third less than the theoretical average requirement, but these girls were both very large for their ages, in fact, had nearly attained adult stature and accordingly did not need the number of calories for growth usual for that age.

On the whole, it would seem that the curves suggested are approximately correct for the average caloric requirements up to the age of 11 years. We feel confident that a larger number of observations for the later years will verify the estimates for those years also.

When the individual observations are considered on a per kilo basis and compared with the proposed curves for calories per kilo, the individual observations show wide variation, but practically all the high values for calories per kilo were found in case of very

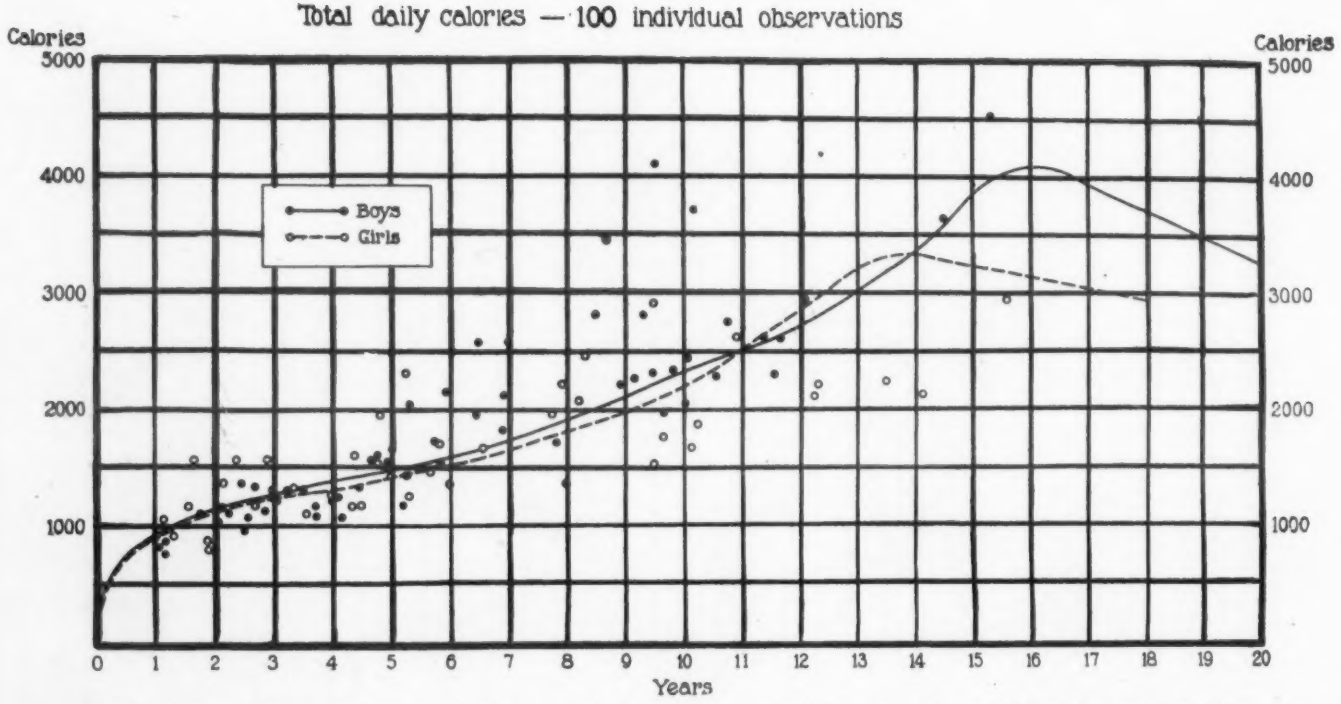

Fig. 7.—Curved lines represent suggested total daily calories according to age, the solid line the curve for boys, the broken line for girls. The dots represent the calories taken in individual observations on boys, the circles those taken by girls.

active children or those who were very much under weight for their height or undersize for their age. The values which were found to be much lower than the average shown by the curves were mostly in case of quiet children or those who were either large for their age or over weight for their height.

SUMMARY

1. In calculating the total caloric requirements of children there must be considered separately the component parts of which the total is made up. These are the requirements for basal metabolism, for growth, for muscular activity and the food values lost in the excreta.

2. The basal requirements, which have been determined by Benedict and Talbot, are highest per kilo at about nine months and steadily fall from this time up to adult life.

3. The food value normally lost in the excreta is a nearly uniform proportion of the intake, about 10 per cent., for all ages after infancy.

4. The requirements for growth are greatest during the period when growth is most active, namely, during the first year of life and during adolescence. They are nearly uniform from the fourth to the tenth or eleventh years.

5. The average for three factors—basal, growth requirements and food values lost in excreta—are nearly uniform for children of the same weight living under similar conditions.

6. The requirement for activity is the only factor which varies widely with different individuals.

7. The great differences in the calculations of different writers who have estimated theoretical values for total calories per kilo for children are in part due to the fact that they have not sufficiently considered the different component parts which make up the total.

8. The average caloric requirement of children according to our observations is about 100 calories per kilo at an age of 1 year (about 9.5 kilos). For boys it falls to about 80 calories at 6 years (about 20 kilos) and remains practically constant at this value up to the age of 15 years, the increasing requirements for activity being met by the reduction in basal requirements per kilo. After a weight of 50 kilos (about 15 years), is reached the calories per kilo can rapidly be reduced to adult standards, about 48 calories per kilo. The requirement for girls falls to 76 calories per kilo at 6 years (about 20 kilos), continues at this value until the tenth year. During the tenth year it rises because the basal requirement is nearly constant while there is an increase in needs for growth and activity. The requirement remains at 80 calories per kilo until growth is complete, then falls rapidly to adult standards, about 44 calories per kilo.

9. In our calculation we have allowed a much higher value for calories per kilo during adolescence than have others. This seems to be absolutely essential, because of the increased growth needs at this time and the large requirement for muscular activity.

10. According to our allowance the total daily caloric requirement of children of both sexes during adolescence exceeds by nearly 1,000 calories the requirements of the adult man or woman of moderate activity.

11. Children who are under weight require more calories per kilo than those who are of average weight for their age. Children who are over weight require fewer calories per kilo than those of average weight.

12. The schedule here proposed is a tentative one and is based on present knowledge, which is in many respects incomplete. There are a number of points which must be studied more fully before definite standards can be established.

For the many reasons which we have discussed, it seems the right procedure to allow for children during the period of adolescence more calories than the adult ration and, as growth needs end, to diminish the caloric allowance to the adult standard. We quite agree with Benedict's recent statement, "It is still, however, the best practice to give a most liberal diet to children, since the greater part of the evidence on under weight indicates that children usually receive too little rather than too much food."

CALCIUM IN THE BLOOD OF CHILDREN *

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The publication of several relatively accurate and simple micro-methods for the determination of calcium in the blood has opened the way for many interesting lines of investigation in the field of calcium metabolism. About two years ago, inspired by the acquisition of a new weapon, we embarked on the study of an old and much investigated problem, viz., the calcium metabolism of children. The obvious connection between rickets, and probably infantile tetany, and some error of calcium metabolism, has naturally led us to lay special stress on the study of patients suffering from these disorders, but we also have attempted to collect data on the calcium content of the blood of children suffering from a variety of pathological conditions.

Our calcium determinations have been made by the method of Lyman,[1] which we have modified in a few minor details. Lyman's method for the determination of calcium in blood consists essentially in the following steps: the removal of protein by precipitation with trichloracetic acid, the precipitation of calcium from the protein-free filtrate, as calcium oxalate, by means of the technic of McCrudden, the transformation of the calcium so precipitated into colloidal calcium stearate, and the nephelometric determination of the same. The experience gained during several years' use of this method has led us to adopt the following modifications: First, the employment of citrated plasma, (0.1 gm. of solid sodium citrate to 10 c.c. of blood), as preliminary experiments convinced us that no calcium was precipitated by the use of this amount of sodium citrate, and that as pointed out by Halverson [2] and his collaborators, the determination of calcium in plasma or serum is of more significance than when made on whole blood as originally recommended by Lyman. Second, the use of a variety of standards for the final nephelometric reading. Lyman recommends the use of a single standard, equivalent to 0.2 mg. of calcium. While this standard is well suited for work with normal material, in cases where the amount of calcium is much reduced, it is impossible to obtain accurate results by its use. We have, therefore, adopted the plan of invariably preparing three standards for every

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* From the Chemical Laboratory and the Children's Medical Service of the Massachusetts General Hospital.

1. Lyman, H.: J. Biol. Chem. **29**:169, 1917.

2. Halverson, J. O.; Mohler, H. K., and Bergeim, O.: J. Biol. Chem. **32**: 171, 1917.

determination, or series of determinations. These standards are made up to contain 0.20, 0.15, and 0.10 mg., respectively, of calcium. If this assortment of standards is provided it is always possible to obtain readings within 20 per cent. of the unknown, whereas, if only one standard is made, many determinations must be discarded simply because of the wide deviations between the reading of the standard and that of the unknown. The magnesium determinations were made by a method recently described by one of use.[3]

In Table 1 we have collected the results obtained from the examination of 119 samples of blood taken more or less at random from patients in the children's ward of this hospital. These figures are arranged according to the level of plasma calcium without regard to the diagnosis.

Such a series of analyses is of value in that they furnish a fair idea of the variations to be expected in unselected hospital material. An inspection of these results shows a maximum figure of 13.5 and a minimum of 1 mg. of calcium per hundred c.c. of blood plasma, figures which represent an enormous range. Further analysis gives the distribution as shown in Table 2.

It is to be regretted that we were unable to make observations on strictly normal children. It may safely be assumed that many of our cases were normal in so far as there existed any possibility of the presence of an abnormality of calcium metabolism, but as these subjects were inmates of a hospital ward we scarcely feel justified in collecting such cases into a "normal" group.

For comparison we have to rely on a series of figures obtained on twenty-two normal adults in which the maximum figure was 12.1 mg., the minimum 7.2 mg. and the average 10 mg. of calcium per hundred c.c. of plasma.

Howland and Marriott [4] found that the calcium per hundred c.c. of serum was between 10 and 11 mg. in five normal infants.

It would seem useless to attempt to discuss separately and in detail the results obtained on the very considerable number of pathologic conditions represented by the figures given in Table 1. We shall, therefore, confine our discussion to the findings in those conditions in which there is at least a theoretical possibility that some abnormality of calcium metabolism may exist.

In this group rickets and infantile tetany are, perhaps, the most important, although there seems to be a possibility that some abnormality may exist in pneumonia, nephritis and, perhaps, in certain conditions associated with delayed blood coagulation.

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3. Denis, W.: J. Biol. Chem. **41**:363, 1920.
4. Howland and Marriott: Quart. J. M. **11**:10, 1918.

TABLE 1.—CALCIUM PER 100 C.C. BLOOD PLASMA SHOWING THE VARIATIONS

No.	Sex*	Age	Season	Diagnosis	Calcium per 100 C.c. Plasma, Mg.	Magnesium per 100 C c. Plasma, Mg.
1	♀	1 yr.	Winter	Microcephalus, delayed mental development	13.5	....
2	♂	4 mo.	Spring	Regulation of feeding	12.9	1.00
2a	♂	1½ yr.	Winter	Lobar pneumonia	12.1	....
3	♀	7½ mo.	Autumn	Pyelitis	11.6	....
4	♂	7½ yr.	Summer	Bronchopneumonia, foreign body in ear	11.3	....
5	♂	10 mo.	Summer	Scurvy	11.2	....
6	♂	3 mo.	Autumn	Regulation of feeding (artificial mixed)	10.8	....
7	♂	11 mo.	Spring	Bronchopneumonia, colitis	10.6	1.20
8	♂	3 mo.	Summer	Necrosis of alveolar process of right maxilla	10.5	....
9	♂	21 mo.	Summer	Indigestion with fermentation	10.4	....
10	♀	3 yr.	Winter	Hypertrophied tonsils and adenoids, cervical adenitis	10.4	....
11	♀	10 yr.	Summer	Purpura hemorrhagica, chronic	10.2	....
12	♀	7 mo.	Spring	Pharyngitis; retropharyngeal abscess; cervical adenitis; otitis media; congenital heart; rickets; secondary anemia	10.1	2.20
12a	♀	7 mo.	Spring	Same as above	10.1	2.20
13	♀	4 yr.	Summer	Sarcoma of kidney	10.0	....
14	♂	2 mo.	Autumn	Regulation of feeding (breast)	10.0	....
15	♀	3½ yr.	Winter	Retarded mental and physical development as result of previous encephalitis	9.9	....
16	♀	4 mo.	Winter	Regulation of feeding, nephritis	9.8	1.2
17	♂	6 yr.	Summer	Hydrocephalus decompression	9.7	....
18	♀	7 mo.	Autumn	Microcephalus; hare lip; convulsions (?)	9.7	....
19	♀	10 mo.	Spring	Lobar pneumonia	9.7	....
20	♂	1 yr.	Winter	Bronchitis; cleft palate; hare lip	9.6	2.0
21	♂	3 mo.	Summer	Regulation of feeding	9.6	....
22	♀	9 mo.	Winter	Scurvy	9.6	....
23	♂	6 yr.	Summer	Lobar pneumonia	9.6	....
24	♀	10 mo.	Summer	Feeding; indigestion, carbohydrate; impetigo contagiosa	9.4	....
25	♂	?	Summer	....	9.3	....
26	♂	2 yr	Autumn	Epilepsy; retarded mental development	9.2	....
27	♀	16 mo.	Summer	Unresolved pneumonia; Tb. bronchial lymph nodes (+ von Pirquet); adenoids; rickets; congenital syphilis ?	9.1	....
28	♂	5 yr.	Winter	Neoplasm of lung; died Nov. 7, 1919	9.1	....
29	♀	2½ yr.	Summer	Infectious diarrhea	8.8	....
30	♀	6½ mo.	Autumn	Acute fermental diarrhea; cellulitis scalp	8.8	....
30a	♀	7 mo.	Autumn	Same as above	8.8	....
32	♂	2¼ yr.	Summer	Bronchial glands; rickets	8.8	....
33	♀	11 mo.	Winter	Amaurotic family idiocy	8.8	....
34	♂	23 mo.	Winter	Foreign body in left bronchus; atelectasis	8.6	....
35	♀	6 mo.	Spring	Regulation of feeding	8.5	2.58
36	♀	8 yr.	Winter	Laryngismus stridulus (thymic asthma)	8.4	....
37	♀	11 mo.	Summer	Congenital syphilis; otitis media; cervical adenitis; died Aug. 28 1919	8.4	....
38	♀	6 mo.	Spring	Regulation of feeding, same as No. 35	8.3	2.55
39	♀	6 yr.	Winter	Catarrhal jaundice	8.3	....
40	♂	4 mo.	Winter	Regulation of feeding	8.2	....
40a	♂	3 mo.	Spring	Convulsions (?) of cerebral or intestinal origin	8.2	....
41	♂	4 mo.	Spring	Regulation of feeding	8.1	1.6
42	♀	10 mo.	Spring	Rickets; bronchopneumonia (?); enlarged thymus; clubbed fingers	8.0	1.60
43	♂	3 wk.	Winter	Congenital stenosis of pylorus	8.0	....
44	♂	7 mo.	Summer	Regulation feeding; pylorospasm	8.0	....
45	♀	8 mo.	Autumn	Intestinal indigestion due to carbohydrate	8.0	....
46	♂	9 mo.	Autumn	Rumination; intestinal indigestion due to starch	8.0	....
47	♂	6 yr.	Winter	Catarrhal jaundice	8.0	....

* In this column, ♂ indicates male, and ♀ female.

TABLE 1.—CALCIUM PER 100 C.C. BLOOD PLASMA SHOWING THE VARIATIONS—(*Continued*)

No.	Sex	Age	Season	Diagnosis	Calcium per 100 C.c. Plasma, Mg.	Magnesium per 100 C.c. Plasma, Mg.
48	♀	14 mo.	Autumn	Regulation of feeding (artificial).....	8.0	....
49	♂	6 yr.	Autumn	Tb. meningitis, cerebral; died Sept. 22, 1919.....	8.0	....
50	♀	4 mo.	Winter	Chronic intestinal indigestion due to sugar malnutrition.....	7.9	....
51	♀	15 mo.	Winter	Bronchitis (?); lobar pneumonia.....	7.7	2.0
52	♂	11 mo.	Autumn	Rickets; spasmophilia (?).....	7.7	....
53	♂	1 yr.	Winter	Acute bronchitis.....	7.7	....
			2 da. later	Acute bronchitis.....	7.7	....
54	♀	2 yr.	Winter	Bronchopneumonia.....	7.6	....
55	♀	22 mo.	Summer	Pyopneumothorax; pyelitis.....	7.6	....
55a	♂	7 yr.	Summer	Mitral insufficiency and stenosis; abrasion on chin.....	7.6	....
56	♀	3½ mo.	Winter	Chronic intestinal indigestion due to sugar malnutrition (see No. 50).....	7.4	....
57	♂	8 mo.	Winter	Regulation of feeding; bronchopneumonia; congenital syphilis.....	7.3	3.2
58	♂	1 yr.	Summer	Rickets; regulation of feeding.....	7.2	1.27
59	♀	1 yr.	Summer	Splenomegaly; secondary anemia.....	7.2	....
60	♂	14 mo.	Winter	Diarrhea; acute otitis media; bronchopneumonia.....	7.2	....
61	♂	17 mo.	Winter	Lobar pneumonia.....	7.2	....
62	♂	5½ yr.	Winter	Acute nephritis; follicular tonsillitis; cervical adenitis, chronic.....	7.1	....
63	♀	6 wk.	Summer	Amaurotic idiocy (?); convulsions; regulation feeding.....	6.9	0.8
64	♀	10 mo.	Winter	Chronic intestinal indigestion.....	6.9	....
65	♀	9 mo.	Winter	Bronchopneumonia (?); tuberculosis; tetany.....	6.8	2.0
66	♀	9 yr.	Summer	Migraine; eyestrain.....	6.8	....
67	♀	7 yr.	Autumn	Progressive degeneration of cerebellum.....	6.6	....
68	♂	4 yr.	Autumn	Hypernephroma with metastasis.....	6.6	....
69	♀	5 yr.	Winter	Acute bronchitis.....	6.6	....
70	♀	4 yr.	Summer	Purpura.....	6.5	0.96
71	♂	3 yr.	Winter	Influenza; rickets; strabismus.....	6.5	2.7
72	♂	2 yr.	Summer	Measles; bronchopneumonia; morbilli.....	6.4	....
73	♂	3 yr.	Summer	Acute meningitis; optic atrophy; hypopituitarism.....	6.4	....
74	♀	5 yr.	Autumn	Influenza; bronchopneumonia (?); meningismus; died Sept. 23, 1919....	6.4	....
75	♂	3½ yr.	Summer	Encephalitis.....	6.3	1.60
76	♀	3 mo.	Winter	Regulation of feeding (artificial mixed).....	6.3	....
77	♀	2 yr.	Winter	Otitis media (acute suppurative); rickets.....	6.3	....
78	♀	7 mo.	Winter	Influenza; bronchopneumonia.....	6.1	1.6
79	♀	11 mo.	Spring	Resolving bronchopneumonia (rachitis).....	6.1	....
80	♂	29 mo.	Winter	Bronchopneumonia; congenital syphilis; rickets; iodid rash.....	6.1	....
81	♀	9 mo.	Summer	Bronchopneumonia; pyelitis.....	6.1	....
82	♀	5 mo.	?	Tb. meningitis; miliary tuberculosis; dead.....	6.0	....
82a	♀	22 mo.	Spring	Laryngismus stridulus.....	6.0	....
83	♂	5 yr.	Summer	Acute rheumatic fever; tonsillitis.....	6.0	....
83a	♂	10 mo.	?	Chronic meningitis.....	6.0	....
84	♂	8 yr.	Summer	Hypertrophied tonsils and adenoids; chorea; tonsillectomy.....	6.0	....
85	♂	21 mo.	Spring	Tuberculosis; peritonitis.....	5.8	2.55
86	♂	4 mo.	Summer	Regulation of feeding.....	5.6	1.29
87	♂	11 mo.	Winter	Regulation of feeding (artificial mixed); pyelitis (?).....	5.5	....
88	♂	3 yr.	Winter	Epilepsy.....	5.5	....
89	♀	7 yr.	Summer	Purpura; furunculosis, multiple.....	5.3	1.20
90	♀	8 mo.	Winter	Convulsions; bronchopneumonia; impetigo; secondary anemia; rickets	5.3	0.80
91	♂	9 mo.	Winter	Regulation of feeding (artificial mixed); indigestion due to sugar...	5.2	....
92	♂	10 mo.	Winter	Hypertrophied tonsils and adenoids; spasmophilia (tetany).....	5.2	....
93	♂	8 yr.	Autumn	Acute lymphatic leukemia.....	5.2	....

TABLE 1.—CALCIUM PER 100 C.C. BLOOD PLASMA SHOWING THE VARIATIONS—(*Continued*)

No.	Sex	Age	Season	Diagnosis	Calcium per 100 C.c. Plasma, Mg.	Magnesium per 100 C.c. Plasma, Mg.
94	♂	6 wk.	Summer	Birth injury (intracranial); bronchopneumonia; died Aug. 21, 1919	5.1	....
95	♂	6 mo.	Spring	Bronchitis; bronchopneumonia (acute intestinal indigestion)	5.0	5.0
96	♀	17 mo.	Summer	Lobar pneumonia; pyelitis; empyema (progressive)	5.0	1.55
97	♀	4 yr.	Spring	Epilepsy	5.0	1.0
98	♂	2 yr.	Winter	Congenital heart; ulcerative stomatitis	5.0	....
99	♂	23 mo.	Summer	Intestinal indigestion	4.8	....
100	♂	7 yr.	Summer	Chorea	4.8	1.28
101	♂	10 mo.	Winter	Paralysis of 7th, 12th and 10th cranial nerves; miliary tuberculosis	4.7	2.4
102	♂?	3 mo.	Spring	Nasopharyngitis (?); (enlarged thymus	4.6	2.5
103	♂	4 yr.	Summer	Empyema	4.5	....
104	♂	5 yr.	Autumn	Lobar pneumonia	4.4	....
105	♂	4 mo.	Spring	Regulation of feeding; pylorospasm	3.8	....
106	♂	4½ mo.	Autumn	Chronic infectious diarrhea	3.4	....
107	♀	6 mo.	Winter	Influenza; bronchitis; reflex convulsions; died	3.2	....
108	♂	4 mo.	Spring	Regulation of feeding	3.1	1.00
109	♂	5 yr.	Summer	Petit mal	3.0	1.60
110	♂	5 mo.	Winter	Regulation of feeding; tetany	2.9	0.48
111	♂	7 mo.	Spring?	Rickets; tetany; laryngospasm; died in an attack	2.5	1.28
112	♂	5 mo.	Winter	Convulsions; regulation of feeding; tetany	2.5	1.0
113	♂	5 mo.	Winter	Same as above	2.0	1.0
114	♂	10 mo.	Spring	Bronchopneumonia; tuberculosis (?); rachitis; dead	<2.0	3.2
115	♂	10 mo.	Summer	Rachitis; regulation of feeding; tetany (?); microcephalus	+1.00	1.29
116	♂	4 mo.	Summer	Regulation of feeding	+1.00	1.29

TABLE 2.—DISTRIBUTION OF CALCIUM IN VARIOUS CASES

Mg. of Calcium per 100 C.c. Blood Plasma	Number of Cases	Per Cent. of Total
13.5-12	3	2.5
12 -10	11	9.1
10 - 8	29	24.2
8 - 6	42	35.0
6 - 4	23	19.2
4 - 1	12	10.0

In Table 2 are presented the results obtained on the blood of 28 cases of rickets, seven in the acute and twenty-one in the convalescent stage. While in some of these cases the calcium values are distinctly below normal, the interpretation of the results is somewhat complicated by the fact that several of the patients whose blood gave low calcium values were also suffering from other maladies (pneumonia predominating), which might also affect the calcium level in the blood. No conclusions can, therefore, be drawn from these figures because, as will appear in a later table, changes are found in the blood in many cases of pneumonia.

TABLE 3.—CALCIUM PER 100 C.C. BLOOD PLASMA IN CASES WITH RICKETS

Acute Stage

No	Sex*	Age	Diagnosis	Epiphyses	Rosary	Mg. Calcium per 100 C.c.	Mg. Magnesium per 100 C.c.
114	♂	10 mo.	Rickets; bronchopneumonia....	Slight +	Marked +	<2.0	3.2
101	♂	10 mo.	Rickets; miliary tuberculosis...	Slight +	Moderate +	4.7	2 4
90	♀	8 mo.	Rickets; convulsions; bronchopneumonia	+	Moderate +	5.3	0.8
82	♀	5 mo.	Miliary tuberculosis; rickets....	Slight +	Marked +	6.0	...
79	♀	11 mo.	Bronchopneumonia; rickets....	Moderate +	Marked +	6.1	...
58	♂	12 mo.	Rickets.....	Slight +	Well marked	7.2	1.27
42	♀	10 mo.	Rickets; bronchopneumonia....	Large	Marked	8 0	1.60

Convalescent Stage

103	♂	4 yr.	Empyema.....	0	Slight +	4.5	...
99	♂	23 mo.	Intestinal indigestion.....	0	Slight +	4.8	...
95	♂	6 mo.	Bronchopneumonia.....	0	Slight +	5.0	5.0
85	♂	21 mo.	Tuberculous peritonitis.....	0	Slight +	5.8	2.55
83	♂	5 yr.	Acute rheumatism.....	0	Slight +	6 0	...
81	♀	9 mo.	Bronchopneumonia.....	0	Slight +	6.1	...
77	♀	2 yr.	Otitis media.....	+	+	6 3	...
72	♂	2 yr.	Bronchopneumonia.....	Slight +	Slight +	6 4	...
71	♂	3 yr.	Influenza.....	Slight +	Moderate +	6.5	2 7
68	♂	4 yr.	Hypernephroma.....	0	Prominent	6.6	...
57	♂	8 mo.	Congenital syphilis; bronchopneumonia.....	0	Moderate +	7.3	3.2
55	♀	22 mo.	Pyelitis; pneumothorax.....	Slight +	Slight +	7.6	...
35	♀	6 mo.	Regulation feeding.....	Slight +	Slight +	8 3, 8.5	2.55, 2.58
32	♂	2¼ yr.	Enlarged bronchial glands.....	Slight +	Slight +	8.8	...
30	♀	6½ mo.	Fermental diarrhea.....	0	Slight +	8.8	...
29	♀	2½ yr.	Infectious diarrhea.....	0	Slight +	8.8	...
27	♀	16 mo.	Tuberculous bronchial glands..	0	Slight +	9.1	...
24	♀	10 mo.	Indigestion.....	Moderate +	Moderate +	9.4	...
22	♀	9 mo.	Scurvy.....	0	Def. +	9 6	...
12	♀	7 mo.	Otitis media; secondary anemia	Slight +	Slight +	10.1	2.2
5	♂	10 mo.	Scurvy.....	0	Marked +	11.2	...

* In this column, ♂ indicates male, and ♀ female.

TABLE 4.—CALCIUM PER 100 C.C. BLOOD PLASMA IN CASES OF TETANY

No.	Sex*	Age	Diagnosis	Mg. Calcium per 100 C.c.	Mg. Magnesium per 100 C.c.	Remarks
116	♂	4 mo.	Acute tetany.....	+1.00	1.29	
115	♂	10 mo.	Acute tetany; rickets; microcephalus	+1.00	1.29	
112	♂	5 mo.	Acute tetany; convulsions.....	2.5	1.0	
113	♂	5 mo.	Acute tetany; convulsions.....	2.0	1.0	Same as No. 112 after 13 days treatment
111	♂	7 mo.	Acute tetany with laryngospasm.....	2.5	1.28	Died in attack
110	♂	5 mo.	Acute tetany.....	2.9	0.48	
108	♂	4 mo.	During treatment and convalescence.	3.1	1.00	Same as No. 116, 5 and 19 days after calcium treatment
86	♂	4 mo.	During treatment and convalescence.	5 6	1.29	Same as No. 108
92	♂	10 mo.	Subacute tetany.....	5.2	...	
65	♀	9 mo.	Subacute tetany.....	6.8	2.00	
52	♂	11 mo.	Subacute tetany.....	7.7	...	
82a	♀	22 mo.	Laryngismus stridulus.....	6.0	...	

* In this column, ♂ indicates male, and ♀ female.

In Table 4 are collected the results of our observations in ten cases of infantile tetany, and in Table 5 are detailed the results obtained on patients with convulsions, but without evidence of the presence of tetany. A diagnosis of tetany was made in our cases when carpopedal spasm, Chvosteck and Trousseau signs were present. This was confirmed in most of the cases by a lowered threshold of electric irritability.

TABLE 5.—Calcium Per 100 C.c. of Blood Plasma in Cases Having Convulsions without Evidence of Tetany

No.	Sex*	Age	Convulsions Without Evidence of Tetany	Mg. Calcium per 100 C.c.	Mg. Magnesium per 100 C.c.
107	♀	6 mo.	Reflex convulsions; influenza; bronchitis	8.2	...
90	♀	8 mo.	Convulsions; bronchopneumonia	5.3	0.8
40a	♂	3 mo.	Convulsions of cerebral origin (?); intestinal (?)	8.2	...
83a	♂	10 mo.	Chronic meningitis	6.0	...
			Epilepsy		
109	♂	5 yr.	Petit mal	3.0	1.6
97	♀	4 yr.	Epilepsy	5.0	1.0
88	♂	3 yr.	Epilepsy	5.5	...
26	♂	2 yr.	Epilepsy, retarded mental development	9.2	...
			Chorea		
100	♂	7 yr.	Chorea	4.8	1.28
84	♂	8 yr.	Chorea; tonsils and adenoids	6.0	....

* In this column, ♂ indicates male, and ♀ female.

In some of the cases in Table 4 the content of calcium in the serum is extremely low, while in a few of the more chronic cases it approaches normal values.

These figures are much lower than those of Howland and Marriott,[4] who found in active tetany an average of 5.6 mg., the lowest figure being 3.5 mg.

Calcium chlorid, 25 grains, three times daily were given in two cases of tetany and an increase in the blood calcium resulted which in one case (Cases 116, 108 and 84), was very marked. Associated with this increase of the calcium in the blood serum was the disappearance of symptoms and apparently complete cure. Denis and Minot [5] recently published the results of experiments on the administration of calcium by mouth to men, cats and rabbits. The results of this work indicate that in most cases it is impossible to increase the concentration of calcium in the plasma by ingestion of calcium salts, but that in cats and rabbits where the initial concentration is low, it is sometimes possible to greatly increase the amount of calcium in the plasma by feeding calcium salts.

5. Denis and Minot: J. Biol. Chem. **41**:357, 1920.

Our cases of convulsions not due to tetany (Table 5) showed, on the whole, lower figures than those found by Howland and Marriott. This was particularly noticeable in the cases with epilepsy in which three out of four cases showed less than 6 mg., while none of their cases showed less than 8.9 mg.

TABLE 6.—Calcium and Magnesium Per 100 C.c. Plasma in Lobar Pneumonia, Bronchopneumonia and Acute Bronchitis

No.	Sex *	Age	Diagnosis	Mg. Calcium per 100 C.c.	Mg. Magnesium per 100 C.c.	Temperature, F.	Duration of Pneumonia
2a	♂	1½ yr.	Lobar pneumonia	12.1	...	99-100	After crisis
19	♀	10 mo.	Lobar pneumonia	9.7	...	101-105	4 days
23	♂	6 yr.	Lobar pneumonia	9.6	...	106	8 days
61	♂	17 mo.	Lobar pneumonia	7.2	...	98.6	2 da. after crisis
96	♀	17 mo.	Lobar pneumonia	5.0	1.55	106	2 weeks
104	♂	5 yr.	Lobar pneumonia	4.4	...	103	6 days
4	♂	7½ yr.	Bronchopneumonia	11.3	...	99	2 weeks
7	♂	11 mo.	Bronchopneumonia	10.6	1.2	103	13 days
42	♀	10 mo.	Bronchopneumonia; rickets	8.0	1.6	101	Weeks ?
54	♀	2 yr.	Bronchopneumonia	7.6	...	104-98.6	7+ days
57	♂	8 mo.	Bronchopneumonia; congenital syphilis	7.3	3.2	102	5 days
60	♂	14 mo.	Bronchopneumonia; diarrhea	7.2	...	102	3 days
65	♀	9 mo.	Bronchopneumonia	6.8	2.0	103	20 days
72	♂	2 yr.	Bronchopneumonia; measles	6.4	...	102	4-5 days
78	♀	7 mo.	Bronchopneumonia; influenza	6.1	1.6	104	10 days
79	♀	11 mo.	Bronchopneumonia; rickets	6.1	...	99	
80	♂	29 mo.	Bronchopneumonia; rickets	6.1	...	101-103	4 days
81	♀	9 mo.	Bronchopneumonia; rickets	6.1	...	99	8-10 days
90	♀	8 mo.	Bronchopneumonia; rickets; convulsions	5.3	0.8	99-103	
95	♂	6 mo.	Bronchopneumonia; rickets	5.0	5.0	105-100	4 days
114	♂	10 mo.	Bronchopneumonia; rickets; died	<2.0	3.2	103	4 days
51	♀	15 mo.	Acute bronchitis; ? lobar pneumonia	7.7	2.0	99	
53	♂	1 yr.	Acute bronchitis	7.7	...	99	
69	♀	5 yr.	Acute bronchitis	6.6	...	99-100	

* In this column, ♂ indicates male, and ♀ female.

In Table 6 we have collected the results obtained in twenty-five cases including lobar pneumonia, bronchopneumonia and acute bronchitis. Here, again, some very low figures were obtained. That the calcium content of the blood in pneumonia may be diminished has been suggested by the work of von Moraczewski [6] and Peabody,[7] At the time that these earlier works were done the large amounts of blood required for the analysis prevented the collection of any considerable amount of data so that in the opinion of investigators themselves the findings are more suggestive than definite. Peabody's findings are especially suggestive because he found that during pneumonia there was a calcium retention and after the crisis there was calcium excreted from the body. The blood calcium during the fever, however, was lower than the blood calcium after the crisis. In our cases there was no definite relation between the fever and the amount of

6. von Moraczewski: Virchows Arch. f. Path. Anat. **155**: 1899.
7. Peabody: J. Exper. M. **17**:71, 1913.

blood calcium found in bronchopneumonia. In lobar pneumonia, the figures are also inconclusive but there is a tendency for the blood calcium to be higher after the crisis.

SUMMARY

As the result of a series of observations of the calcium and magnesium content of the blood of 119 children, we have found that a low calcium content of the serum frequently occurs in infantile tetany, acute rickets and in pneumonia. In one case of tetany there was a considerable increase in the blood calcium after the administration of calcium chlorid by mouth. Several cases of epilepsy had a low blood calcium; the significance of these findings is as yet uncertain.

THE ULCERATED MEATUS IN THE CIRCUMCISED CHILD *

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For a number of years my attention has been drawn with increasing frequency to a peculiar lesion of the meatus urinarius occurring only in circumcised male children, and characterized by ulceration, crusting, narrowing of the urinary passage, and nearly always accompanied by painful urination, often with distended bladder, and, occasionally, by hemorrhages. I have been able to find only one reference [1] to it in the literature. While this condition probably is common in occurrence in the experience of all pediatrists, I am inclined to believe that it is more common in this locality and in more recent years than in some other localities and in my own earlier years, and that the manifestations are more severe.

My first impression was that this lesion was caused by rubbing against the clothing of the naturally most accessible and most vulnerable portion of the exposed glans, the meatus. This, however, seemed improbable, for it would hardly explain the deep ulceration often seen, and it was soon evident that similar lesions about the diaper region were not infrequently present at the same time. For a time attention was directed to the narrowness of the meatus as a possible cause, though we soon learned that in doing so we were looking for a cause in what was in reality an effect. Routine examination of the urine gave us no help. Only in the last year or two has the real explanation become increasingly evident. In the twenty-five or more cases seen during the past winter and spring there has been no exception to the observation that this lesion is associated with what is known as the ammoniacal diaper. I had not been aware that anyone had ever reached a similar conclusion, but on looking over Zahorsky's paper [1] on the ammoniacal diaper again I found that he had devoted a paragraph to an excellent description of the lesion in question and had also traced its origin to the ammoniacal diaper. So far as I know this is the only reference to this association in the literature.

While the condition itself is rarely, if ever, of serious import, it is nevertheless usually very troublesome and the apparent general lack of knowledge of its pathogenesis would seem to warrant its presenta-

* Received for publication, July 1, 1920.
* Read at the annual meeting of the American Pediatric Society, May 30 and 31, June 1, 1920.

1. Zahorsky, J.: The Ammoniacal Diaper in Infants and Young Children, Am. J. Dis. Child. **10**:475 (Dec.) 1915.

tion. Its peculiar location, moreover, always causes deep concern in the household.

More commonly the lesion manifests itself as a rather superficial ulceration about the meatus. From what we know about the development of similar ulcers in the diaper region due to the same cause it is probably preceded, as pointed out by Zahorsky,[1] by a vesicle, though this is rarely seen before it is broken. At times the ulcer becomes deep and extensive, up to 2 mm. in depth and more than 5 mm. in width. Usually it is more or less covered by a crust which is very firmly attached over a considerable area. Surrounding the ulcer there is often an area of inflammation which involves both the adjacent surface of the glans and extends into the urethral opening with consequent narrowing. In the severer cases there are commonly present at the same time erythema, vesication and ulceration of the glans, scrotum and the rest of the diaper region wherever the diaper is in intimate contact with the skin.

SYMPTOMS

The symptomatology is evident from the pathology. The salty urine coming in contact with the denuded meatus causes acute pain when the child begins to urinate. He immediately stops urinating and cries with pain. A subsequent attempt to urinate, as the discomfort from a distended bladder forces him to try it again, leads to the same result. No amount of coaxing will induce him to try it again until the distended bladder becomes intolerable or begins to overflow. Then, having once started, the grateful relief that comes from emptying the bladder and the lessening of the pain of the first contact with the urine, will cause him to continue to urinate until the bladder is more or less emptied. Unless the condition is quickly remedied the same cycle repeats itself at the next urination. Often the emptying of the bladder is deferred for from twelve to eighteen hours. As a rule, the condition is less severe than that just described, and the child will urinate before there is very painful distention.

In some cases there is a greater or lesser degree of mechanical obstruction. The urethral opening is nearly always narrowed, often so much so that the urinary stream is threadlike and the urine can be expelled only with evident effort. I have never seen this alone cause serious obstruction. A more frequent cause of nearly complete obstruction is the scab that forms on the ulcerated area. This is very adherent and can hardly be removed without tearing and bleeding of the denuded and adjacent portion of the glans. This is practically always accompanied by a narrowing of the meatus, and it is at times impossible to tell whether the occlusion is due chiefly to the scab or to the narrowing of the urethra itself. Two cases that recently came under observation illustrate these points.

REPORT OF CASES

CASE 1.—A child, aged 2 years, was unable to empty the bladder both because of pain and obstruction and because of overdistention of the bladder. From time to time, there was a dribbling overflow that found considerable difficulty in making its exit. In spite of desperate efforts, aided by coaxing from his mother, he was able only intermittently to force out to a height of two feet two tiny divergent streams no thicker than a fine thread.

Examination showed the meatus completely covered with a firm, dry, parchment-like crust that almost completely occluded the opening, and so firmly adherent that it did not seem expedient to remove it at the time. The bladder was distended almost to the umbilicus. By continuous, gentle pressure over the bladder, and with much coaxing to voluntary effort, we were finally able to empty it almost completely through the two minute openings. If pressure over the bladder was stopped for a moment, the flow would stop immediately as if the bladder had been paralyzed by the overdistention.

CASE 2.—A boy, aged 2½ years, was apparently unable to empty the bladder, probably both because of pain and of great narrowing of the meatus. The opening was barely visible, being so small that it would hardly have admitted a fine needle. The meatus itself was apparently narrowed to this degree and was further covered by a tough skinlike crust that had to be removed, but only at the expense of considerable pain and some blood and adjacent epidermis. Even then the meatus could barely be made out, and it was difficult to see how the bladder could be emptied through it.

A permanent narrowing of the meatus, analogous to a stricture, apparently never occurs even after repeated and prolonged ulceration. In the two cases just cited, after appropriate treatment, the urinary stream was apparently of normal caliber on the following day. The restoration to a normal condition is commonly as rapid as the original production of the lesion itself.

One other symptom occasionally causes great concern to the mother but is never serious. If the ulceration is deep and extensive, there is, at times, a little hemorrhage especially noticed at the end of urination. It is surprising that this does not happen oftener when one considers the great vascularity of the glans.

The ammoniacal diaper that apparently always causes this condition of the meatus is to me still surrounded with mystery in spite of its common occurrence. Clinically it manifests itself as follows. An infant or young child that has, perhaps, attracted no attention to its general health or its state of nutrition, or digestion, except that it is constipated, is noticed when changed at night or in the morning, to have a very strong odor of ammonia about the wet diaper. This odor is not simply one detectable on close effort. The fumes are comparable to those that escape from a bottle of ammonia. They are distinctly irritating to the nostrils, and even cause a biting sensation in the eyes as one stoops over the open diaper. This condition is rarely noticed, except at night and most often toward morning. If the urine of such a child voided later is allowed to stand in a vessel no odor of ammonia is detectable even if it is kept at body temperature.

Sometimes, the condition is present every night, continuously and consecutively, as in a case I saw recently, for over a year. Again, it is apparently absent, or barely noticeable, for weeks and months, only to appear again without any known change in health or in food, with violent manifestations. In one of my own children during the second year the condition would occasionally appear in mild form, then be absent for weeks or months. Suddenly at night, without premonition, or any known provocation, the child would wake up toward morning screaming with pain, the diaper would be almost intolerably strong of ammonia, and the whole diaper region would be reddened and painful as if scalded, and covered with blisters. In a day or so without any treatment the condition would disappear as mysteriously as it came, only to reappear at a subsequent time, perhaps for a longer stay. The condition is apparently much more frequent in private homes than in hospital wards.

Many children have this ammoniacal diaper for weeks and months without any other unpleasant symptoms. Usually it produces at least a local redness and subsequent desquamation of a large part of the diaper region. In severer cases there is scattered vesication and ulceration. These ulcers often remain denuded for a long time, often they heal over but remain as discrete nodules during the whole time that the ammoniacal condition persists. Often the exposed meatus is the only seat of a deeper lesion; rarely it escapes; as a rule, it is involved with the rest of the diaper region.

For the production of skin lesions contact with the wet ammoniacal diaper is apparently always necessary. The word diaper is, of course, here used in a generic sense and includes any article of clothing, or bedding. The skin is always most irritated where the contact is most intimate and prolonged—over the buttocks and lower back, from lying, and across the abdomen and about the thighs above the knees, because of the tighter application of the diaper. The male meatus is peculiarly exposed to such contact, and the delicate mucous membrane is the most vulnerable spot; the female meatus is well protected and is apparently rarely if ever involved. The effect of contact was well illustrated in the first case cited above. For several nights the child did not wet the diaper and the ulcer healed. A few days later he was again unable to urinate because of a new ulceration of the meatus. Without any questioning the mother said that he had wet his underclothing over a small spot with urine and that contact with this spot had apparently brought the trouble on again. The favorable effect that follows dispensing with the diaper at night further confirms this view.

AGE INCIDENCE

The age incidence of this condition is of special interest. It is almost unknown in the nursing baby, though I have seen it in a baby on mixed feeding; is relatively rare in the first six months, and is only exceptionally encountered before the third or fourth month. It is much more common in the latter half of the first year; probably attains its maximum frequency and severity during the second year; becomes less common during the third year, and vanishes soon after this. The lesser incidence after the third year is probably due to the greater infrequency of bed wetting without which it would not be recognizable.

TREATMENT

The treatment of this condition naturally is directed to the lesion itself if it is present, and to the prophylaxis and treatment of the ammoniacal diaper.

If the meatus is ulcerated or crusted over to some extent, and there is no obstruction, the proper therapy would seem to consist in applying thickly some substance like petrolatum that would coat over the involved area so that urination may be less painful and so that there will be protection on contact with the diaper. When the meatus is acutely inflamed, the opening narrowed and covered with an obstructing scab, and urination is difficult and peculiarly painful because of the inflammatory condition, a wet boric acid dressing has always quickly relieved the urgent indications. Gauze wet with the solution is fluffed over and about the penis, this is covered with a thick layer of cotton extending beyond the gauze to keep it in place, and over this the diaper is pinned snugly. The gauze is kept wet with the solution and is changed after each urination. The relief from this procedure has been unfailing and almost instantaneous. Dispensing with the diaper at night often has a favorable effect in preventing new lesions and in allowing old ones to heal. Mechanical dilatation has never been necessary. Neither has catheterization, which would be strongly contraindicated unless absolutely unavoidable.

If the scab itself is causing obstruction, or if it can be removed without injury to the adjacent tissues, this should be done. This is facilitated by the previous application of petrolatum or a wet dressing.

The cautious application of a very weak solution of cocain to the ulcerated area in case the child will not urinate because of pain would seem rational and unobjectionable, though the remembrance of a former attempt to urinate might lessen its usefulness.

The prophylaxis of the ammoniacal diaper presupposes a knowledge of its pathogenesis. To my mind we do not possess this knowledge at the present time with complete clarity.

The more inviting theory is that based on the work of Keller and others that in certain nutritional disturbances due to the ingestion of cow's milk fat beyond the infant's tolerance there is produced a relative acidosis of enteric origin which manifests itself in the urine in the excretion of a hypernormal amount of ammonium salts. This view has been formally championed by Southworth,[2] who reported a number of cases presenting this clinical picture and the patients were relieved of this symptom when the fat was reduced to an adequate degree. He also reported a similar result from the administration of alkalies, favoring potassium, calcium and magnesium bases over those of sodium. The cases detailed by Southworth were nearly all in younger infants in whom there was a definite clinical picture of overfeeding with fat or with milk and the therapeutic results would seem to leave little doubt as to the nature of the primary condition that produced the ammoniacal diaper in these cases.

I am inclined to believe that this explanation may be accepted as one factor in the case of younger infants fed exclusively on the bottle. This might further explain the greater frequency of this condition in my own cases for it has been my practice in recent years to give relatively more milk and less carbohydrate in the bottle feedings than formerly. In fact, the condition has been so frequent in my own cases that I have even assumed it to be within the range of normal and have used no measures to relieve it unless there was definite skin irritation. Even in these cases, however, where a dietetic relationship seems most evident I have been struck by the frequency with which neither reduction of the fat by lessening the milk or by taking off the cream nor the use of alkalies leads to an appreciable therapeutic result.

It seems to me, however, quite impossible on this hypothesis alone to explain the occurrence of the ammoniacal diaper in a very large number of cases. It is, for example, a well known fact that the ammoniacal diaper occurs with greater regularity when dried milk is used than with almost any other food. In my own experience, the severer manifestations, such as vesication and ulceration, occur more frequently in older children who are on a liberal diet and are getting very little milk. One of the most severe and protracted cases I have seen with extensive ulceration of the meatus, scrotum, and, in fact, of the whole diaper region, was in a child, aged 2½ years, that was on a general diet and getting only a pint of skimmed milk. In some cases the mothers have stated that these older children were getting practically no milk at all. Cutting down the milk or removing the cream, even to a marked degree, has in the case of older children been

2. Southworth, T. S.: The Ammoniacal Diaper and Its Correction, Arch. Pediat. **30**:10 (Oct.) 1913.

quite disappointing from a therapeutic standpoint. The use of alkalies has given the same impression.

DISCUSSION

It is interesting in this connection to note that the ammoniacal diaper occurs less frequently and less severely with cream mixtures than with simple whole milk mixtures, or even, as has been pointed out, with dried skimmed milk mixtures. If this observation is correct, then the fat alone cannot account for the condition. This is further borne out by the relative freedom from this symptom when albumin milk is given in spite of its high fat content. It will be recalled that Czerny and Keller's "milchnährschaden," which is apparently due to an excess of fat in the infant's food and in which there is a heightened urinary excretion of ammonium salt, is produced when whole milk is fed in excess of tolerance. Certainly, it does not occur as definitely with cream mixtures, in spite of the fact that fat is assumed to be the factor that causes it. It will be recalled further that Czerny and Keller state that the soap stool does not occur with cream mixtures and they offer the ingenuous explanation that this is due to the fact that it is difficult to get cream that is not "zersetzt," that is, unfavorably influenced by bacteria.

To me it seems more reasonable that while the symptom under discussion may be due to the fat, at least in that class of cases where there is clinical evidence of overfeeding with fat, that fat will cause it only in certain combinations, and only if certain other food elements are represented in certain relative ratios to the fat. Thus, in a milk mixture it occurs less frequently if the fat is relatively higher than the protein and the salts as compared with their normal relative representation in whole milk; and more frequently if the normal proportion is maintained, or even if the fat is relatively lower than the protein and the salts. The fact is not sufficiently emphasized that the different food elements cannot be considered as isolated factors but must always be considered in relation to the other food elements in the causation of clinical pictures.

While the fat within these limitations may account for an increased excretion of ammonium salts in a certain proportion of these cases, and may thus supply one factor in the pathogenesis of the ammoniacal diaper, I do not believe that it accounts for all or most of them. Even in those cases where the fat would seem most clearly the causal agent, it is impossible to exclude the protein, or even the salts as a factor. I have gained the impression that, in the production both of the clinical picture of "milchnährschaden," and of the ammoniacal diaper, it is not so much a matter of amount of fat as of the amount of

milk even if it is partly skimmed. The protein and the salts, if this observation is correct, would command attention and especially, of course, the protein. This would explain many phenomena that cannot be accounted for on the assumption that the fat is the main factor. It would explain the frequency of the ammoniacal diaper when Dryco Milk is used in spite of its low fat content because as commonly used the amount of protein is relatively considerably higher than with ordinary fresh milk mixtures. Assuming that a milk from which two thirds of the fat has been removed is reduced to about one eighth or one ninth its volume in the process of desiccation, and that eight level tablespoonfuls of the dried product represent one ounce by weight, then one level tablespoonful would equal approximately one ounce of fresh milk, skimmed to a nearly equal extent. In giving two and one-half or even three tablespoonfuls of the dried milk to each pound of baby, as is commonly done, one would give the protein and salt equivalent of at least from 2½ to 3 ounces of milk to the pound of baby which would represent a much larger amount than is ever used in feeding fresh milk. This might also explain the greater frequency of the occurrence of the ammoniacal diaper in my own experience in more recent years during which I have been feeding more milk, that is, more protein and less carbohydrate. On this basis, too, one might find a satisfactory explanation for those cases in older children that are on a nearly general, almost fat free, diet.

The failure of ammonuria to occur, except in connection with the wet diaper in situ, together with the peculiar behavior of the ammoniacal diaper would suggest a further nondietetic factor residing in the diaper itself. A hyperexcretion of ammonium salts cannot alone be assumed to account for the ammoniacal diaper. We have here not combined but free ammonia. The ammonium salts that would be present in this condition are fairly stable, and it is very doubtful whether the evaporation of the urine would be carried to a point where ammonia would be liberated to the extent found in these diapers. It is well known that certain alkalies break up ammonium salts and liberate free ammonia. On this basis Zahorsky,[1] after failure to combat the condition by lessening the fat in the food and by the use of alkalies therapeutically, came to the conclusion that "the immediate cause of the ammoniacal diaper is the presence of an alkali in the diaper, or the bedding." This alkali he traced to "strong alkaline soap that had not been rinsed thoroughly from the diapers, or bedding, or to the presence of an alkaline stool, or to the possible presence of lime in the dried diaper in locations like St. Louis where the lime content of the water is high."

Zahorsky's explanation was distinctly appealing in that it alone, apparently, could account for the mysterious vagaries of the ammo-

niacal diaper; the startling appearance and sudden disappearance without known change in food or in health; the invariable association with the wet diaper in situ only; the failure of dietetic and alkaline treatment in many cases; and the greater incidence and severity of the symptom in older children which he also noted. Unfortunately he contented himself with saying: "It is not necessary to give the details" and presented no evidence. That soap, lime, and an alkaline stool do not explain the condition in a great many cases can easily be demonstrated by excluding these factors experimentally.

Other agents, however, may produce the same result and the action of bacteria naturally suggests itself. Thus in a recent personal communication Zahorsky says: "The diaper or the bedding, infected by an enormous number of bacteria, not boiled daily, must also be considered." The thought would suggest itself further that bacteria might liberate ammonia, not directly or indirectly from the ammonium salts in the urine, but from the urea. It is well known, for example, that *Micrococcus ureae*, and probably also other organisms in the urine, act on urea with the liberation of ammonia. As suggested by Kendall in a personal communication, the large evaporating surface presented by the diaper as compared with the small surface in the test tube would naturally lead to the freeing of a comparatively larger amount of ammonia. These considerations would lead us back again to the clinical impression already recorded that the determining factor in those cases in which the dietetic factors are easily grasped is the amount of milk given even if skimmed; that is, of protein, rather than, say, the amount of fat. More milk carries with it more protein and an increased excretion of urea for bacteria to act upon.

The further question would naturally arise whether a hyperexcretion of ammonium salts, or of urea, due to an excess of either the fat or the protein in the diet, is a prerequisite to the production of the ammoniacal diaper; or whether something in the diaper itself is sufficient to elicit the condition in a normal urine. So far as I know, the answer to this question is not yet at hand. The fact that free ammonia occurs with great regularity with certain foods, and an excessive amount of fresh milk such as Dryco milk, would point to the conclusion that the diaper alone is not sufficient to bring out this symptom unless there is an abnormal urinary condition. The occurrence in older children on a general diet makes it hard to assume an abnormal urinary factor and would suggest that the diaper can cause it even if the urine is normal. The invariable association of this symptom with the diaper would again suggest the diaper as the important factor and especially in these cases where the symptom occurs erratically. Some further observations made by Zahorsky are interesting but inconclusive in this connection. He found that "the ammo-

nia content of the urine was relatively higher in older children than in infants," and "while rather high in children presenting this symptom (ammoniacal diaper) not higher than in many who did not present it." He found further that "all but one of the patients so examined," that is, those having ammoniacal diapers, "showed the ammonia nitrogen higher in the morning after the night's rest." The fact that the ammoniacal diaper is rare in hospital cases as compared with those in private practice can be accounted for on either basis. In hospitals all diapers are thoroughly sterilized for obvious reasons, while in homes this is commonly omitted. On the other hand, it is also true that hospital babies, as a rule, can stand less milk than babies in private practice and so the dietetic factor is reduced to a minimum.

While our knowledge of the whole subject lacks precision and finality, nevertheless it gives us a definite line of treatment. The prophylaxis of the ammoniacal diaper and so of the ulcerated meatus, in accordance with our present state of knowledge, would consist then, in the avoidance of an excess of milk in the diet and a compensating use of the more tolerable carbohydrates, the dextrin-maltose preparations in younger infants, and these together with the starches in older infants. The treatment would consist in the reduction of the amount of milk; the increase, if permissible, of the carbohydrates; together with the use of such alkalies as milk of magnesia, lime water, or potassium salts. In selected cases malt soup best meets all of these indications. In older children on a general, nearly milk free diet, the dietetic treatment is still baffling in my own experience. The indications on the part of the diaper would be met by thorough rinsing and thorough boiling daily of all diapers and night clothes, possibly even the bedding.

The bearing of this lesion on the question of circumcision is perhaps evident.

CONCLUSIONS

1. An ulcerated meatus in the circumcised child only is a frequent symptom.

2. The "ammoniacal diaper" is the cause of this lesion.

3. The etiology of the "ammoniacal diaper" is still obscure but seems due to one or both of two factors: a dietic error that increases the ammonium or urea content of the urine, and the presence of an alkali or of certain bacteria in the diaper.

4. The treatment consists in correcting, if possible, the dietetic error and in thorough rinsing and boiling of the diapers, night clothes and bedding.

A STUDY OF TUBERCULOSIS IN INFANTS AND YOUNG CHILDREN *

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From April 1, 1914 to April 1, 1920, 8,919 sick children were admitted to the Babies' Hospital. Among them were 359, or 4 per cent., who had symptoms of tuberculosis in some form; while three others had tuberculous lesions at necropsy which had not been suspected during life. In all then, 362 children with tuberculosis were admitted. During these six years 2,024 necropsies were performed, and 184, or 9 per cent., were on tuberculous subjects. By comparison with two previous studies,[1] in which respectively 13 and 16 per cent. of the children coming to necropsy were found to have tuberculosis, there has been an actual reduction in the number of children showing tuberculous lesions at necropsy during the past six years. That is, 184 of 2,024 necropsies showed tuberculosis in the years from 1914 to 1920, while from 1908 to 1914 there were 178 of 1,320 necropsies which disclosed tuberculous lesions. The number of children admitted with tuberculosis has decreased slightly, from 5.04 per cent. during the period of the first study (1898 to 1908), to 4.15 per cent. during the period of the second study (from 1908 to 1914), and again to 4.06 per cent. in the period from 1914 to 1920. At the same time, the total death rate for all admissions to the Babies' Hospital has decreased, while the death rate for cases of tuberculosis has increased. Since the percentage of necropsies permitted is greater at present than it was a decade ago, the decrease in the number of necropsies on tuberculous subjects, in spite of the higher death rate for tuberculosis, is significant.

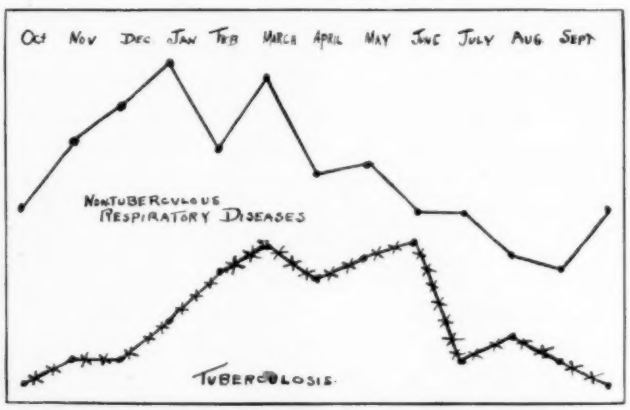
From the figures of Table 1 it would seem that tuberculosis is slowly decreasing among the class of infants and young children in New York City from which the Babies' Hospital draws its admissions. The decrease may be ascribed to a combination of several factors, important among which are the education of mothers in the hygiene

* Received for publication, Aug. 4, 1920.
* From the laboratory of the Babies' Hospital.

1. Wollstein, M.: The Distribution of Tuberculous Lesions in Infants and Young children, Arch. Int. Med., **3**:221 (Feb.) 1909. Wollstein, M., and Bartlett, F. H.: A Study of Tuberculous Lesions in Infants and Young Children, Based on Postmortem Examinations. Am. J. Dis. Child. **8**:362 (Sept.) 1914.

of the infant and the home, and better provision for isolation and care of adults with tuberculosis, since the great majority of cases of infantile tuberculosis is caused by the human type of tubercle bacillus. While care of the milk supply is of gravest importance, the fact that only a small percentage of this country is infected with the bovine type of tubercle bacillus shows that it is not the prime factor in the reduction in the number of cases of tuberculosis which our studies show.

The curve of incidence of cases of tuberculosis plotted according to the month of admission, shows that the greatest number occurred from February to June inclusive, and the lowest number during the second half of the year. In comparing tuberculosis with the non-tuberculous respiratory infections, it becomes apparent that the number of tuberculous patients increases as the respiratory infections subside



Comparison by months of admissions of cases of nontuberculous respiratory diseases with tuberculosis. The latter increase as the former lessen in number.

(see chart). The connection between the two is obvious. The general resistance of children who are exposed to tuberculosis is markedly diminished by an acute respiratory infection of whatever cause, especially if pneumonia occurs. In consequence, a latent tuberculous focus may become active, or an acute tuberculous infection may be acquired.

HISTORY OF EXPOSURE

A definite history of exposure was obtained for only ninety-four of 362 children in our series. There were twenty-nine tuberculous mothers; thirty-seven fathers had the disease; seven grandparents were the source of infection, while eight children contracted the disease from sisters and brothers, eleven from aunts and uncles, and two from friends. It is interesting to note that the youngest infants were infected by the mother. One child, aged 6 weeks, and two aged 8

weeks, were exposed to tuberculous mothers. Twenty-two of twenty-nine children whose mothers were tuberculous died before they were 1 year old; six died in the second year of life and only one boy was three years old at the time of his death. Fathers, on the contrary, come into less intimate contact with the young infants, and only sixteen of the thirty-seven whose fathers had tuberculosis died before they were one year old; eleven lived to be over 2 years old, while one reached the age of 5 years. The youngest infant who contracted tuberculosis from the father was 4 months old. Infection from other relatives occurred in only fourteen children under one year of age, or half of the twenty-eight so exposed.

TABLE 1.—INCIDENCE OF TUBERCULOSIS AS DIAGNOSED CLINICALLY AND AT NECROPSY

Time	Number of Admissions	Cases of Tuberculosis Admitted	Number of Necropsies	Cases of Tuberculosis Found at Necropsy	Death Rate for All Admissions, per Cent.	Death Rate for Tuberculosis Cases, per Cent.
1889 to 1908	9,165	462	1,131	185 or 16.4%	31.3	82.2
1908 to 1914	7,467	310	1,320	178 or 13.5%	32.2	86.8
1914 to 1920	8,919	362	2,024	184 or 9%	28.0	93.0

It must be remembered that a negative family history is of comparatively little value, and by no means always true.

AGE

In age the 362 children in our series ranged from 6 weeks to 5 years as follows:

TABLE 2.—INCIDENCE OF TUBERCULOSIS BY AGES

Under 3 months	3
Between 3 and 6 months	41— 44 under 6 months, 12 per cent.
Between 6 and 12 months	95—139 under 1 year, 38 per cent.
Between 12 and 18 months	76
Between 18 and 24 months	49—264 under 2 years, 73 per cent.
Between 2 and 3 years	46—310 under 3 years, 86 per cent.
Between 3 and 4 years	31
Between 4 and 5 years	12
Five years	9— 52 over 3 years, 14 per cent.

No case of congenital tuberculosis came under observation. Of the children admitted with tuberculosis 73 per cent. were under 2 years of age, and only 14 per cent. were over 3 years of age. The greatest frequency was noted in children between 6 and 12 months

old. Rabadeau-Dumas [2] found that the ages of 8 months and 2 years, respectively, supplied the largest number of cases of tuberculosis among young children.

RACE

There were more tuberculous children of American parentage (155) admitted to the hospital than of any other one nationality. Sixty-four children were of Italian parentage; the parents of 36 were Irish, 34 were from Austria-Hungary; 30 from Russia; 14 were Germans; 7 English; 3 Spaniards and 3 Roumanians. The parents of 57 per cent. of these children were foreign born, and only 43 per cent. were born of Americans, including 12 per cent. who were negroes.

Without entering into a discussion of the value of the von Pirquet skin test, it may be remarked that 269 of the 362 children in the series, or 74 per cent., gave a positive reaction; fifty did not react, and in forty-three cases the reaction was not recorded.

Clinically, the cases were grouped as follows: 193 patients had tuberculous meningitis, 28 had tuberculous peritonitis, 116 had pulmonary and general miliary tuberculosis, 2 had intestinal tuberculosis without peritonitis, 10 had cervical adenitis, 12 had tuberculosis of the bones, and one infant had genital tuberculosis following circumcision. All but 24 of the children died, and 184 came to necropsy (Table 3). The nonfatal cases were those with tuberculosis of the fingers, knee, hip, vertebrae or cervical glands who were discharged from the hospital, and of which final outcome is unknown.

TABLE 3.—CLINICAL FORMS OF TUBERCULOSIS AMONG 362 CHILDREN ADMITTED TO BABIES' HOSPITAL

	Cases
Tuberculous meningitis	193
Tuberculous peritonitis	28
Pulmonary and general miliary tuberculosis	116
Intestinal tuberculosis without peritonitis	2
Tuberculous cervical adenitis	10
Tuberculosis of the bones	12
Tuberculosis of penis and inguinal glands	1
Total	362

The necropsies include 123 cases of meningitis, five of peritonitis, fifty-four of pulmonary tuberculosis, and two cases of intestinal tuberculosis without peritonitis.

Grouping the necropsies according to the oldest lesion found in the body, we have classified the cases into those which were primary in the respiratory and digestive tracts, respectively. In several

2. Rabadeau-Dumas, L.: Tuberculosis in Children, Progrés. méd. **34**:312, 1919.

instances, the lesions seemed to be about the same age in both, so that it was impossible to group them with accuracy. One case of genital tuberculosis following circumcision did not come to necropsy.

TUBERCULOSIS PRIMARY IN THE RESPIRATORY TRACT

In some of these cases the oldest lesion was found in the lungs, in others in the bronchial glands, and in still others the lesions in the lungs and in the glands seemed to be about the same age. The first group, with the oldest lesion in the lungs, comprised seventy-four cases. Calcareous areas in the lungs were noted in only three instances. Cavities, usually of small size, were present in forty lungs examined, or in 21 per cent.

The primary lesion was found more often in the upper than in the lower lobes, and was present almost as frequently in the left upper (sixteen times) as in the right upper (seventeen times) lobe. It occurred in the right lower lobe thirteen times, in the left lower lobe sixteen times and in the right middle lobe eleven times. As in previous studies of cases in this hospital the right lung was found affected more frequently (forty-two times) than was the left (thirty-two times).

There was no instance in which the lung alone was the seat of a tuberculous lesion. In one case there was only a small tuberculous nodule with a calcareous center in the left upper lobe and a calcareous nodule in one bronchial lymph node. This occurred in a child 9 months old, who died of bronchopneumonia following diarrhea, without any clinical evidence of tuberculosis. Another child of 3 years had one small, tuberculous, cheesy nodule, surrounded by a few recent tubercles, in the left upper lobe, while several bronchial lymph nodes contained tubercles with cheesy centers. This child died of a simple bronchopneumonia. Tuberculosis was discovered at necropsy.

The bronchial glands contained the primary lesion in fifty-seven cases: thirty-five times on the right side; eleven times on the left side; seven times the glands on both sides were equally involved; and four times the oldest lesion was in a gland at the bifurcation of the trachea. Calcareous nodules were present in the bronchial lymph nodes of four children.

In no instance were the bronchial glands alone affected. However, a 3 year old child had two cheesy tubercles in one bronchial lymph node at the root of the left lung, and the pia mater was the only other structure involved in the tuberculous process. In this hospital it is only in older children that tuberculous meningitis has been encountered without generalized tuberculosis.

Lesions apparently of equal age in both the lungs and the bronchial nodes were seen in thirty-six cases, three times with calcareous degeneration in both gland and lung.

TUBERCULOSIS PRIMARY IN THE DIGESTIVE TRACT

The digestive tract was the seat of the primary lesion in nine cases which came to necropsy. The mesenteric glands contained the oldest tuberculous focus in the body seven times. In one infant the mesenteric glands and the intestines showed lesions of apparently equal age, and in another the cervical glands presented the oldest lesion. Only three of these nine children showed no evidence of tuberculosis in the lungs or bronchial glands. In two the lungs were free, but tubercles were found in a bronchial gland. There were four children whose lungs contained recent miliary tubercles, while their bronchial nodes were free. Evidently the route of infection was through the blood stream in these cases. In only five of the 184 necropsies were the lungs not involved, and in only seven were the bronchial glands not the seat of tuberculous lesions.

Lesions of about equal age were found in the respiratory and in the digestive tract in seven instances, three times with calcareous areas present in both the mesenteric and bronchial lymph nodes. Such cases suggest that at the time of exposure the tubercle bacilli were both swallowed and aspirated.

TUBERCULOUS MENINGITIS

Tuberculous meningitis was present in 53 per cent. of the children in this series; none recovered. The patients were from 9 weeks to 5 years of age; 39 per cent. were under 1 year and 76 per cent. under 2 years of age; that is, 40 per cent. of the infants in our series who contracted tuberculosis died of meningitis before they were 2 years old. Necropsies were performed in 123 cases of tuberculous meningitis. In 116, the primary lesion was found in the respiratory tract, and the children were evidently infected by aspirating the tubercle bacilli. Three children who died of meningitis had the primary lesion in the intestines and mesenteric nodes, and they must have been infected by ingestion of the bacilli. One of these three cases occurred in a female infant, 9 months old; the cervical glands became infected during the fourth month of life and were incised one month later. She developed tuberculous meningitis in the ninth month and the tubercle bacilli in the spinal fluid were proven to be of the bovine type, which is a much rarer cause of meningitis than is the human type of tubercle bacilli. The infant had been nursed

during the first two months of life and then fed on raw cow's milk. This seems to be clearly a case of food infection.

There were four cases of tuberculous meningitis in which the lesions seemed equally old in both the respiratory and the digestive tracts. In these cases the bacilli were swallowed and aspirated at the time of exposure.

That tuberculous meningitis is usually associated with a generalized tuberculosis is shown by the fact that the average number of organs containing tuberculous lesions was nine in babies under 6 months old, and from seven to eight in infants aged from 6 months to 2 years. An exception to this rule has been cited.

The youngest infant with tuberculous meningitis in this series was only 9 weeks old. The mother had active pulmonary tuberculosis, consequently the baby was nursed for only three days and was then fed raw cow's milk. A cough developed when the patient was 6 weeks old, and symptoms of meningitis 3 weeks later. Tuberculids appeared on the skin of the chest and abdomen. At necropsy a very generalized tuberculosis was found, involving the skin, pia mater, pleura, lungs, bronchial and mediastinal lymph nodes, pericardium, thymus gland, liver, spleen and kidneys. A cavity in the right upper lobe seemed to be the oldest lesion. This infant presented a very typical picture of aspiration tuberculosis contracted from his mother, becoming generalized within two months and terminating with meningitis at the age of 71 days.

TUBERCULOUS PERITONITIS

There were twenty-eight cases of tuberculous peritonitis in this series. Only five came to necropsy. Laparotomy was done on three of the children and tuberculous masses were reported in the abdomen of each. The youngest of these twenty-eight children was 5 months old; only four were less than 1 year old; six were 3 and 4 years old; that is, only 36 per cent. of the children in our series who had tuberculous peritonitis were under 1 year old, while 64 per cent. were beyond their second year.

The peritoneum is more often involved in the tuberculous process in older children than in young infants. The youngest infant (aged 5 months) who had tuberculous peritonitis showed, at necropsy, a calcareous area in a mesenteric node as the oldest focus of a tuberculosis which had become generalized and which involved the liver, spleen, stomach and intestines, while the lungs and bronchial glands showed only recent tubercles. In two of the peritonitis patients, aged 13 months and 2½ years, respectively, the lungs were entirely free of any tuberculous lesion and infection was limited to the abdomen.

In one case, a child 3 years old, it was not possible to locate the primary focus, because the lungs contained a large cavity, the bronchial and mesenteric lymph glands were enlarged and cheesy, and the intestinal ulcers were numerous, large and deep.

Tuberculous peritonitis and tuberculous meningitis occurred in a little girl aged 3 years, who gave no history of exposure to tuberculosis. An operation for an abscess of the appendix at the age of 2½ years was followed by an unhealed sinus. A second operation, five months later, showed the presence of tuberculous mesenteric lymph nodes, tubercles on the peritoneum and adhesions between the coils of the intestines. Meningitis developed three weeks later and resulted in death after one week. At necropsy all the mesenteric lymph glands were found to be cheesy and many of them contained calcareous areas, while the bronchial nodes were neither enlarged nor cheesy. Miliary tubercles were present in the lungs, liver and spleen, and old ulcers were found in both the large and small intestines. The mesenteric nodes were the seat of the primary lesion.

THE HEART

The heart is rarely involved in tuberculosis in young children. In cases with very generalized lesions, both in young infants and in children over 2 years of age, recent small gray tubercles are sometimes found on the visceral pericardium, more rarely on the endocardium, especially over a pectinate muscle, or in the myocardium. Tubercles in the heart are rarely more than six in number and usually there are only from one to three. Occasionally, the ascending arch of the aorta may be the seat of tubercles. In our series tubercles were seen in the visceral pericardium in eleven cases, on the endocardial lining five times, and in the heart muscle five times. In two cases small tubercles were present on the surface of the aorta just above the origin of the vessel.

Exudative tuberculous pericarditis is very rare, only one case occurring among the 184 necropsies studied. This condition is of such interest and infrequency that a detailed report seems desirable. A boy, 11 months old, developed pulmonary tuberculosis after an attack of pertussis when 7 months old. At necropsy the pericardial sac measured 7 cm. across the base and 9 cm. from base to apex. The visceral and parietal layers were adherent by means of a cheesy exudate from one to two cm. in thickness, which enveloped the entire heart, completely obliterating the pericardial cavity. The myocardium of the left ventricle was 2 cm. thick, and of the right ventricle 1½ cm. thick. A yellowish cheesy layer in both ventricular walls occupied all but the innermost 3 or 5 mm. of myocardium. There was a

large cheesy cavity in the right lung, while miliary tubercles were present throughout both lungs and in the pia mater, liver, spleen, bronchial and mesenteric glands.

SKIN

Tuberculids of the skin were found in only four of our cases, all young infants, aged 8 weeks, 3 months, 5 months and 13 months, respectively. The three youngest patients died of tuberculous meningitis. All had a very generalized tuberculosis.

SUMMARY

This study emphasizes the following facts:

1. The great frequency of tuberculosis in infancy and early childhood.
2. The suggestive decline of tuberculosis among the young children admitted to the Babies' Hospital during the last six years.
3. The greater incidence of tuberculosis of infants and young children acquired by inspiring tubercle bacilli compared with that acquired by swallowing the bacilli with milk or food.
4. The rapid generalization of tuberculosis in young subjects, the rapidity and degree of generalization being, as a rule, in inverse proportion to the age.
5. The great frequency with which termination by tuberculous meningitis occurs.
6. The absence of any case of healed tuberculosis from this series of 184 necropsies on tuberculous children.

THE FAT CONTENT OF FECES OF YOUNG CALVES*

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New-born calves excrete feces during the first week of life which show distinct variations in the gross appearance. A study was made, therefore, of the amount of fat present in the feces, from birth to the time when the calves were approximately a week old. It is during this time that the calf readjusts its metabolic activities from that of an intra-uterine existence to one in which it subsists by absorption from its gastro-intestinal tract. It was found in general that the fat content of feces increases from birth to approximately the third day, after which it decreases and assumes an approximately normal level. At the time of the high fat content, there is present in the feces a greater proportion of fatty acids in the form of soap, indicating a lack of absorption on the part of the young animal.

METHOD

The method used for the determination of fat was a modification of the method developed by Saxon,[1] which is in itself a development of the method of Meigs, for the determination of fat in feces. It seemed advisable to estimate the quantity of soap present in feces, as well as the total fat and fatty acids present as free fatty acids and soap. To do this we first extracted moist feces with ether and alcohol, according to the Saxon procedure, and then to the residue added hydrochloric acid to liberate the fatty acids from the soaps. The ether layer when removed contains a small amount of alcohol and acid; it was, therefore, collected in a separatory funnel and washed with distilled water until free from chlorids. This precaution is necessary to prevent the formation of ethyl esters of the fatty acids present. Comparative analyses showed this procedure to give, with suitable precautions, the same results as in the Saxon procedure.

After we had commenced our analyses, the modification of the Röse-Gottlieb method by Holt, Courtney and Fales[2] appeared. These investigators applied a somewhat similar procedure to dried feces, by extracting with combined ether and petroleum ether. They derived their value for soaps by subtracting the results obtained by a nonacid

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* From the Department of Animal Pathology of the Rockefeller Institute for Medical Research.

1. Saxon, G. J.: J. Biol. Chem. **27**:99, 1914.

2. Holt, L. E.; Courtney, A. M., and Fales, H. L.: Am. J. Dis. Child. **17**:38 (Jan.) 1919.

extraction from that obtained by an acid extraction. When such a procedure is applied to work with fresh feces we do not obtain results comparable with those obtained by a second extraction, i.e., fat is obtained through the second extraction which does not appear in the first extract.

From our experiences with this modified Saxon method for the determination of fat and for the distribution of neutral fat, fatty acids and soap in feces, we have found that the method gives consistent results for total fat. When used for the estimation of fatty acids and for the estimation of soap and free fatty acids as we have modified it, the method gives fairly satisfactory results. In feces of a high fat content, rich in soap, the double extraction tends to give low results for total fat, but the loss appears to be in neutral fat rather than in the fatty acids and soap. We had hoped to develop the double extraction method to such an extent that we could dispense with the acid extraction but found it necessary to continue our determination according to the Saxon procedure as well as our own as a check on the results. For the acid alcohol-ether extraction the method in detail is as follows:

From 5 to 6 grams of thoroughly mixed moist feces are weighed into a 100 c.c. glass stoppered cylinder, as suggested by Saxon. A small amount of water is added, and the cylinder is shaken to obtain a thorough mixture of feces and water. Then from 1 to 2 c.c. of concentrated hydrochloric acid is added and the volume made up to 30 c.c. Twenty cubic centimeters of ether and 20 c.c. of alcohol are added and the contents shaken for five minutes after each addition. After the last shaking the cylinder is allowed to stand until the ether-fat layer separates. The ether is blown off into a separatory funnel, containing a small amount of water. Four portions of ether of 5 c.c. each are added successively, the contents agitated, and the ether layer removed.

A second portion of 20 c.c. is then added and the contents shaken for five minutes. This layer is then removed and four 5 c.c. portions are again added and removed. The ether extract is thoroughly washed with water until free from chlorids, transferred to an Erlenmeyer flask and the ether removed by evaporation on a hot plate. The fat residue is then extracted with petroleum ether, boiling below 60 C., and the extraction filtered through a small fat free filter paper, into a weighed flask. The petroleum ether is removed and the fats dried at approximately 90 C. to constant weight. Fifty cubic centimeters of benzol are added to the weighed fat, heated to boiling, and immediately titrated with tenth normal potassium alcoholate. This procedure gives the total fat and fatty acids, present as free fatty acids or soap.

Double Extraction.—The procedure in this case is practically identical with that just described with the following exceptions:

(a) Extraction without Acidification: In the first original extraction the hydrochloric acid is omitted, and the ether extract is passed through a fat-free filter to retain any particles of soap which may be carried over with the ether.

(b) Acidification and Extraction: The residue remaining from the extraction under (a), plus the filter paper from (a), is acidified with from 1 to 2 c.c. of hydrochloric acid and the extraction repeated as outlined. The results obtained under (a) above represent most of the fat and the free fatty acids. The extraction under (b) contains the residual fat, if any, and the fatty acids present as soaps.

We have found that it is necessary to work with fresh feces because when the feces are kept for any length of time there is a gradual transformation of fat into fatty acid as well as rearrangements in the fatty acid-soap equilibrium. One of the largest possible sources of error, as indicated by Holt, Courtney and Fales, is in mixing the feces to obtain a thoroughly representative sample for analysis.

Moisture was determined by weighing from 5 to 7 gm. of moist feces into a weighed lead cap and drying in a vacuum desiccator over sulphuric acid. The hydrogen ion concentration was determined colorimetrically on a filtered water extract of the moist feces using the indicators and standard solutions of Clark and Lubs. Nitrogen was determined by the Kjeldahl method.

SUBJECTS

The animals studied were born at the Institute and kept in stalls separate from their mothers. They were taken to the dam to suckle twice a day, night and morning, or were fed milk from the dam from a pail.

Three calves did not receive colostrum but were given a mixed whole milk. With the exception of number 456 B, which was a Guernsey, all animals were either grade or purebred Holsteins.

COLLECTION OF FECES

The feces were collected in glass jars at the time of defecation. The collections were not quantitative. Analyses were begun soon after collection.

DATA

Data were obtained from fourteen calves, over periods ranging from four to twenty-four days for each animal. Additional preliminary data on samples of feces obtained from different calves at various ages show results similar to those presented as to the sequence of changes in the same calf.

The data are contained in Tables 1 and 2. The results for fat, fatty acids and soap are expressed as percentages, in terms of the moisture-free substance and the nitrogen as percentage of the moisture and fat free substance.

The data show an increase in the fat content from birth to approximately the third day, after which the fat content decreases to a somewhat lower and fairly uniform value. Associated with a high fat content on the third day is noted an increased percentage of soaps.

The physical character of the feces corresponds somewhat to the variation in fat content, the meconium is usually greenish black in color; it may consist of hard balls, or it may be soft and rich in mucus; quite often the latter type of stool follows the former type. Succeeding the meconium are feces yellow in color and of a more or less pasty consistency, often containing fatty acid crystals. This is the stool most characteristic of approximately the third day. Following this is the fairly soft stool, greenish brown in color, the type of feces which persists unless a digestive disturbance occurs. The separation between the two types of feces was very marked—when the two types appeared in the stool they could, as a rule, be differentiated readily.

The fat-soap mixture remaining after titration of the fatty acid was examined for nonsaponifiable material. From 6.1 gm. of fat, fatty acids and nonsaponifiable matter 0.17 gm. of nonsaponifiable material was obtained, representing approximately 2.8 per cent. of the mixture. This value is undoubtedly high. The nonsaponifiable material was largely cholesterol.

During the time that calves are showing the change in the appearance and composition of feces they are receiving a variable diet. The first milk or colostrum is rich in protein and the colostral bodies but is not, according to published analyses,[3] appreciably richer in fat than milk secreted after lactation has proceeded for some time. The colostral bodies do carry the fat in the form of larger droplets than occur in milk.

It seemed possible that the colostrum itself might be responsible for the character and composition of feces passed during the first three days. Three calves, 487 B, 495 B, 474 B were, therefore, fed the whole mixed milk from cows well along in the period of lactation. In all cases the meconium was passed readily, but subsequent defecation was delayed. Calf 487 B passed meconium on the first day and on the second day a sample consisting largely of meconium with a small amount of yellow pasty feces. A sample was not obtained, nor so far as we could determine was passed, between the second and

3. Eckles, C. H., and Palmer, L. S.: Research Bull. 25, Missouri Agric. Exper. Sta., 1916; König., Chem. Nährungs u. Genussmittel, **1**: 1903.

TABLE 1.—Composition of the Feces of Young Calves

(Fat percentage of the dry sample. Nitrogen as percentage of the moisture and fat free sample.)

No.	Age, Days	Solids, per Cent.	Total Fat, per Cent.	Neutral Fat, per Cent.	Fatty Acids as Soap, per Cent.	Free Fatty Acids, per Cent.	N, per Cent.	p_H
657	½	38.4	11.0	9.8	0.1	1.1		
	1	36.0	14.4	13.4	0.1	0.9		
	3	27.0	15.1	7.7	0.9	6.4		
	4	29.7	14.8	8.6	0.9	4.4		
	5	24.5	9.6	7.0	0.4	2.2		
336B	½	40.9	20.1	18.8	0.2	1.2	7.0	
	2 a.m.	39.6	10.5	6.6	1.0	2.9	11.9	
	2 p.m.	38.3	11.5	6.2	2.1	3.2	12.3	
	3	27.3	6.2	4.4	0.0	1.7	12.6	
	4	27.5	7.0	4.1	0.0	2.9	11.6	
479B	½	43.7	15.1	13.7	0.5	1.0		
	1	40.7	9.1	2.8	4.1	2.2	12.5	
	3	34.1	26.1	17.9	1.4	6.8	12.3	
	6	29.3	7.4	3.6	0.2	3.5	11.6	
489B	1	35.1	16.3	15.4	0.3	0.5	7.6	
	2	40.4	11.9	6.3	2.0	3.6	9.9	
	4	28.6	10.6	7.1	0.2	3.4	12.0	
	7	31.3	9.3	4.1	0.2	5.1	9.5	
	9	29.6	5.8	3.3	0.2	2.2	9.0	
488B	1	44.9	3.4	1.6	0.2	1.7	13.6	
	2	43.0	4.1	1.5	0.2	2.4	13.7	
	4	35.9	12.3	5.2	0.5	6.6	12.0	
	5	43.6	14.6	9.1	0.6	4.9	9.6	
	12	21.9	13.9	7.6	0.4	5.9	8.1	
	13	28.1	48.7	23.1	4.4	16.2	7.8	
	20	31.3	21.7	2.8	13.8	5.1	8.3	
759	1	26.5	6.6	6.1	0.1	0.4	....	6.6
	2	36.3	24.9	14.0	6.6	4.4	....	6.2
	3	36.7	16.3	7.6	1.8	6.9	....	5.8
	4	37.1	11.2	4.3	0.3	6.6	....	6.2
	6	26.0	17.2	8.5	0.9	7.6	....	6.2
	7	28.4	13.9	4.9	0.2	8.8	....	6.2
756	2	38.7	20.2	12.6	1.2	6.4	....	6.2
	3	33.1	24.5	4.4	14.0	6.0	....	6.1
	4	33.1	7.8	2.4	0.1	5.4	....	5.6
	6	45.5	7.9	4.7	0.9	2.4	....	5.6
	7	43.4	10.3	6.4	2.2	1.8	....	5.7
	9	33.6	8.5	3.3	0.5	4.7	....	5.6
465B	1	39.7	14.5	12.9	0.3	1.3	7.3	6.7
	2½	33.9	24.0	14.5	3.7	5.7	9.0	6.2
	3½	33.9	37.5	21.1	4.7	11.7	9.5	5.7
	4½	21.8	10.6	5.6	0.0	3.9	10.1	5.7
	6½	33.3	10.8	5.0	0.5	5.2	11.6	5.6
478B	1	43.4	16.6	14.0	0.3	2.3	....	6.9
	2	34.2	33.0	17.8	7.2	8.1	13.4	5.9
	3	32.7	26.4	12.7	5.5	8.1	13.1	5.4
	8	24.5	16.4	10.3	0.6	5.5	13.1	5.6
480B	1	41.2	3.2	1.3	0.0	1.9	20.2	6.4
	2	46.1	7.7	3.0	1.3	3.4	11.4	5.8
	3	38.1	20.7	15.3	2.2	3.3	11.8	5.9
	4 a.m.	33.1	15.5	10.2	1.5	3.8	11.2	6.1
	4 p.m.	34.7	12.8	9.4	0.6	2.8	11.9	
	5	42.0	14.1	7.8	0.5	3.8	9.3	
477B	1	23.9	16.6	10.3	1.2	5.1	12.6	5.9
	2	29.8	19.7	13.4	1.7	4.6	10.0	5.6
	2	37.7	9.2	4.0	1.4	3.8	12.8	5.6
	3	40.7	27.0	19.6	0.7	7.2	10.2	5.8
	7	30.3	19.8	10.7	0.2	8.9	10.0	5.2
Calves Which Did Not Receive Colostrum								
478B	1	40.5	8.7	7.1	0.6	1.1	8.4	
	5	32.1	15.3	5.9	0.3	9.1	8.7	6.8
	6	26.3	51.4	12.4	21.9	16.8	7.5	5.2
	7	26.5	47.3	7.8	21.1	20.2	7.1	6.2
	8	26.6	42.7	4.4	17.5	20.8	6.4	6.4
	11	29.7	22.3	6.6	9.2	6.4	8.2	6.8
	12	28.2	11.7	6.2	1.0	4.4	10.3	6.8
	15	31.7	8.9	6.7	0.0	2.3	8.3	6.6
495B	1	32.5	8.6	7.9	0.3	0.3	6.9	6.8
	7	31.5	16.4	4.6	3.1	8.7	9.9	5.8
	8-9	33.7	18.0	6.3	4.2	8.8	10.4	6.2
	10	28.4	12.8	4.7	3.9	4.3	10.8	
	13	36.2	11.4	5.7	2.3	3.4	8.9	7.2
474B	1	35.6	16.1	14.8	0.3	0.9	7.7	6.8
	5	28.6	13.1	7.1	0.6	5.5	11.3	5.4
	6	25.8	5.6	2.8	0.8	2.2	9.7	6.2
	7	32.4	6.3	3.1	0.0	3.2	9.0	5.4
	8	22.0	9.1	5.3	0.0	3.8	9.0	5.8

fifth days. On the fifth day three stools, small in amount, were passed of approximately the same consistency. An analysis was obtained, on the third sample, the others being unsatisfactory for analysis. These samples were yellow, pasty in consistency similar to those obtained immediately after the meconium. This type of stool was then followed by daily passages of feces, high in fat content and white in color, apparently an abnormal product. It was not until the eleventh day that the character of the feces returned approximately to normal. The other calves, 495 B and 474 B, likewise showed delay of defecation after the passage of meconium. The second sample passed by calf 495 B was obtained on the fourth day after birth but was dropped in the bedding and could not be analyzed. The greenish brown stool ordinarily passed about the fourth day did not appear until the eighth or ninth day. With calf 474 B the second defecation occurred on the fifth day and greenish brown feces appeared on the seventh day. The chemical composition of the feces of these last two calves, if they be considered in the sequence of defecation rather than the actual date after birth on which they were passed, follows somewhat the sequence of changes characteristic of normal feces. We do not feel, therefore, that the increased fat content and high soap is necessarily related to the colostrum.

TABLE 2.—AVERAGE COMPOSITION OF THE FECES OF YOUNG CALVES WITH RELATION TO AGE

Age, Days	Number of Analyses Represented in Average	Solids, per Cent.	Total Fat, per Cent.	Neutral Fat, per Cent.	Fatty Acids as Soap, per Cent.	Free Fatty Acids, per Cent.	N, per Cent.	p_H
1	13	37.6	13.8	10.6	1.1	2.1	11.8	6.4
2	10	38.4	14.4	8.2	2.1	4.0	9.1	5.8
3	9	33.7	22.2	12.3	3.5	6.4	11.5	5.7
4	9	31.3	11.4	6.3	0.4	4.4	11.4	5.9
5	3	36.7	12.7	7.9	0.5	3.6	9.4	
6	4	33.5	10.8	5.4	0.6	4.6	11.6	5.8
7	4	33.3	13.3	6.5	0.7	6.1	9.7	5.7

In addition to the data recorded, tests were made on a filtered water extract of the feces for the presence or absence of coagulable protein. In practically all cases we found protein present which was coagulable with heat and a small amount of precipitate in cold with acetic acid.

In certain cases in which the coagulable protein was particularly rich, this protein was extracted and examined as to its character, as follows: Feces were worked up with distilled water, acidified with acetic acid, centrifugalized, the proteien precipitated with ammonium sulphate, dialyzed and reprecipitated at least three times. Other precipitations were made with saturated sodium chlorid. Two globulins were obtained, one having precipitation limits for ammonium sulphate between 2.8 and 3.4 and precipitated by dialysis, and the other having

precipitation limits between 3.4 and 4.4, and not precipitated on dialysis. Both proteins were coagulable with heat. In addition protein was obtained on complete saturation with ammonium sulphate coagulable with heat.

SOAP IN FECES

Feces obtained during the second to the fourth day were found by our analysis to be rich in soaps, had a peculiar glistening appearance, and when a small portion of such material was suspended in water, in which it was insoluble, it gave an effect such as occurs when finely divided metal is suspended in gasoline. It was also noticed in the course of the nonacid extraction that white particles tend to accumulate between the aqueous layer and the ether-fat mixture.

It appeared possible that we might be able to separate this material, which we assumed to be and subsequently found to be soap, from the associated material. Portions of fecal material were, therefore, subjected to the procedure adopted for the extraction of fat and free fatty acids, i. e., to nonacid extraction, except that this material was kept suspended in the ether layer by agitation and siphoned off before it could settle. The material obtained was then thoroughly extracted with ether in a separatory funnel. When suspended in a 50 per cent. alcohol-water mixture, by varying the proportions of alcohol and ether, we were able to remove fecal material of greater specific gravity than the soap which had been carried over in the original separation. As a result we obtained a product which was practically pure white, but which on decomposition was found to carry a small amount of yellow pigment which was transformed in an acid solution to a green pigment, evidently a bile pigment. These crystals were thoroughly washed with ether, dried and again extracted with ether until no more extractable material could be obtained. The following results obtained on analysis showed the soap to be chiefly calcium stearate.

TABLE 3.—ANALYSIS OF STOOL FOR SOAP

Weight of sample	0.5849 gm.
Weight of fatty acids	0.5216 gm.
Cacium present	0.0369 gm.
Magnesium	Trace
Titration of fatty acids with 0.1144 N. potassium alcoholate	16.34 C.c.
Molecular weight from calcium determination	283
Molecular weight from fatty acid titration	279
Molecular weight of stearic acid	284
Iodin value	3.9
Stearic acid (Hehner and Mitchell)	86%

DISCUSSION

The changes in composition during the first week of the life of calves indicate that there is a readjustment in the metabolic activities of the calf during the first three days. The data obtained suggest a

fairly complete digestion of fat, but a partial failure to absorb it. Whether or not the failure to absorb the fatty acid is due to a specific condition of the intestinal mucosa or to physical or chemical conditions which influence the combination of the fatty acids with calcium has not been determined. It seemed possible that colostrum might in some way be related to this increased excretion of fat and the excretion of soaps. The effect of colostrum was to delay the excretion of fecal material. Examination of the data in relation to the sequence of defecation without reference to time, in the two calves which may be considered as normal, indicate a somewhat higher fat content of the feces immediately following the meconium.

That there are metabolic disturbances during the first days of life, or earlier, are indicated in the work of various authors. Theobald Smith (unpublished notes) has noted in some cases, the presence of protein in the urine of new-born calves, which disappears on approximately the third day. Reusin [4] and Schloss and Crawford [5] have noted a high uric acid excretion in new-born infants which reaches its maximum on approximately the third day. Kingsbury and Sedgwick [6] have noted a similar phenomenon for the blood of new-born infants. Scours occurs in new-born calves ordinarily within the first three days. It seems to us that the increased fat content of the feces of new-born calves on the third day is probably associated with the other readjustments which are taking place in the animal. It is interesting that in a change of diet such as from fasting to a normal diet, metabolic activity is readjusted to the new plane in approximately three days.[7]

CONCLUSIONS

1. Data have been presented showing the presence of a high fat content on approximately the third day in the feces of new-born calves. This high fat content is accompanied by a relatively high percentage of soap.

2. Calves which did not receive colostrum passed the meconium readily but showed a delayed defecation subsequently.

3. From feces of high soap content nearly pure calcium stearate was separated.

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4. Reusin, H. Z.: Geburtsh. u. Gynäk. **32**:36, 1895.
5. Schloss, O. M., and Crawford, J. L.: Am. J. Dis. Child. **1**:203 (Feb.) 1911.
6. Kingsbury and Sedgwick: J. Biol. Chem. **31**:261, 1917.
7. Howe, Mattill and Hawk: J. Am. Chem. Soc. **33**:568, 1911.

CHRONIC TUBERCULOUS HILUS PNEUMONIA IN CHILDREN *

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No disease has received more attention in the literature than tuberculosis, especially pulmonary tuberculosis, yet the subject is by no means exhausted. There is a type of pulmonary tuberculosis infrequently met with in children which is often overlooked, unless constantly kept in mind.

The most frequent form of tuberculosis in children, aside from tuberculous meningitis and miliary tuberculosis, is tuberculous pneumonia, either of the lobar pneumonic or bronchopneumonic type. Chronic tuberculosis as met with in adults is almost unknown in infants and children under 2 years of age. With the aid of the roentgen ray more cases of the chronic and subacute forms are being discovered. (Reuben,[1] Dunn,[2] Eisler,[3] and Wesler and Bass,[4] speak of such cases.)

The type of tuberculosis to which I wish to call attention may be defined as a diffuse or parenchymatous process involving that portion of the lung immediately adjacent to the hilus. It is characterized by a gradual onset, comparatively mild constitutional symptoms, fairly definite physical signs (except early), and, as a rule, ends in recovery.

The mode of entry, as in most other forms of pulmonary tuberculosis, is probably through the respiratory tract, according to the views of Hamburger,[5] Ghon[6] and Dunn[2] in this country. This point is by no means definitely settled.

The pathology is not definitely known. There are no necropsy reports and we only know the roentgen-ray and clinical findings, as determined by physical examination. Early roentgenologic studies reveal considerable enlargement of the tracheobronchial glands. This

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1. Reuben, M. S.: Fever, Initial Sign in Tuberculosis of Children, Arch. Pediat. **33**:171, 1916.
2. Dunn, C. H.: Tuberculosis in Infancy, Am. J. Dis. Child. **11**:85 (Feb.) 1916.
3. Eisler, F.: Die Interlobare Pleuritische Schwarte der Kindischen Lunge im Roentgenbilde, München. med. Wchnschr. No. 35, 1899 (Aug.) 1912.
4. Wessler, H., and Bass, M. H.: Recurrent Hilus Infection in Children, Am. J. Dis. Child. **11**:198 (March) 1916.
5. Hamburger, F.: Die Tuberculose des Kindesalters, Leipzig u. Wien., 1912.
6. Ghon, A.: Der Primäre Lungenherd bei der Tuberculose der Kinder, Berlin u. Wien., 1912.

would speak for a direct extension from the glands into adjacent lung tissue. The process usually assumes a more or less triangular outline, with the base toward the hilus, according to Wesler and Bass, who have studied these cases roentgenologically. The apex has a tendency to follow the interlobar fissure. The lesion is more common on the right side, and the shadow is irregular both as to outline and density in different parts of the lung. There is no great tendency toward cavity formation or calcification. When healing occurs there may be very little evidence of fibrosis or scar formation, either as determined by physical signs or the roentgen-ray examination.

The clinical history is not uniform. The earliest manifestations are irregular fever (Fig. 1), occurring in a child otherwise well, and stationary or slight loss in weight. The early fever in tuberculous children was emphasized by Reuben.[1] It may occur at an early age. One of my patients became ill when 12 months old. Sluka's [7] statement that chronic tuberculosis of this type does not occur under two years does not seem to be without exception. The fever is at first moderate, from 101 to 102 F., and may either be remittent or intermittent. With the fever there is increase in pulse rate, fretfulness and considerable sweating. As the disease progresses, the fever becomes higher, from 103 to 104 F., the pulse becomes more rapid and there may be some gastro-intestinal disturbances, especially in infants when the fever is high. Profuse perspiration is an early and frequent accompaniment of the fever and usually occurs in the early morning hours (Fischberg [8]).

Cough occurs sooner or later. It may be very slight in the early stages and is often overlooked, but it becomes more manifest later. Dyspnea may be mentioned as an early symptom, especially on exertion, as when the child is examined. The child then breathes as if there were some expiratory obstruction, reminding one of the neighing of a horse and somewhat resembling asthmatic breathing.

The physical signs, too, are variable. Early they may be absent or so slight as not to be detected. The first sign in one of my cases was diminished breathing. Frazer [9] gives dulness as the earliest sign of tuberculosis in children. As the disease progresses the dulness and diminished breathing become more marked and distant bronchial breathing also may appear. Râles are often present, especially along

7. Sluka, E.: Die Hilus Tuberculose des Kindes im Roentgenbilde, Wien. klin. Wchnschr., (Feb.) 1912, p. 259; ibid., (Feb.) 1913, p. 254.

8. Fishberg, M.: Pulmonary Tuberculosis, Ed. 2, Philadelphia, Lea & Febiger, 1919; Diagnosis of Pulmonary Tuberculosis in Children of School Age, Med. Rec. **92**:406 (Sept. 18) 1917.

9. Frazier, K.: Early Tuberculosis in Children, Brit. J. Tuberc. **9**:1, 1915.

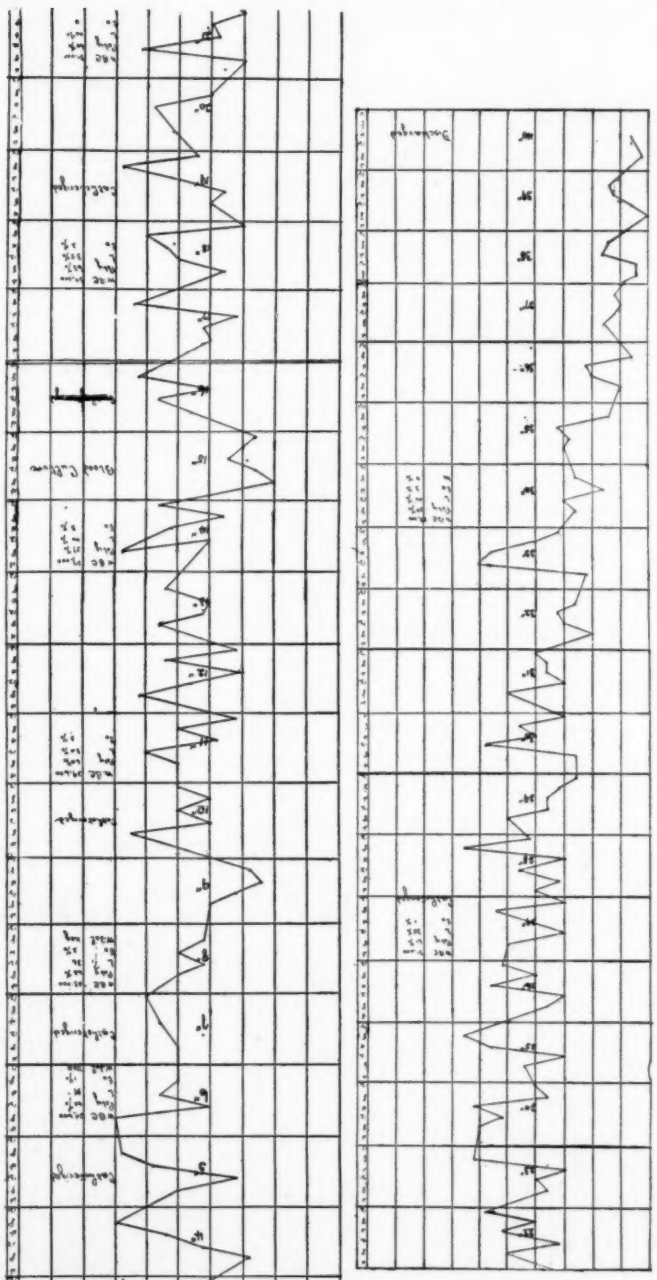

CHART 1.—Case 1

Fig. 1.—Temperature record in Case 1 during the first thirty days of illness.

the margins of the process, when it is extending. Late there usually are râles over the entire lesion. These signs may extend and become so definite that the presence of fluid or large pulmonary abscess is diagnosed. Increased respiration, limitation of expansion, increased fremitus and retraction may also occur. The liver and spleen were enlarged in one of my cases and there were palpable glands in the supraclavicular fossa.

The course of the disease is toward recovery. It may, however, last for many months or even years.

There may be a leukocytosis. There are not many reports as to the blood picture in the literature. My own observations seem to indicate that a high white blood count is not incompatible with tuberculosis in infants and children. In one of the cases here reported the white blood count was persistently high, ranging from 24,000 to 34,000 per c.mm., with a polymorphonuclear percentage of from 64 to 71. The urine may show a trace of albumin, even in the absence of other evidence of renal involvement. There is no particular tendency toward anemia. The sputum is scanty and it requires persistent effort and painstaking examination in order to demonstrate tubercle bacilli. In one of my cases it was only after the twentieth examination that I was able to demonstrate tubercle bacilli in the sputum. Injection of the sputum into a guinea-pig may demonstrate tubercle bacilli earlier. The roentgen-ray findings were discussed under pathology.

The diagnosis may be made more often if Hamberger's [5] dictum, "think of tuberculosis when no other diagnosis can be made," and the possibility of this kind of tuberculosis, is kept in mind. Given a child with prolonged irregular fever, even without definite lung signs, tuberculosis should be suspected. When in addition to the fever there is dulness and diminished breathing and only an occasional cough, or dyspnea, tuberculosis must be considered until ruled out. The following diagnostic points are relied on: (1) Von Pirquet; (2) sputum examination; (3) roentgen-ray examination; (4) lung puncture, and (5) enlarged supraclavicular glands.

Von Pirquet: The von Pirquet is of more value than it is generally believed to be. Frazer [10] regards it as of distinct value even up to the tenth year. Veeder and Johnson [11] are of the same opinion. It certainly is of great value up to 2 years of age.

Sputum Examination: The presence of tubercle bacilli found either by direct examination or on guinea-pig inoculation, makes the diagnosis.

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10. Frazer, T.: The Significance of the von Pirquet, Med. Rec. **87**:57, 1915.
11. Veeder, B. S., and Johnson, M. R.: The Frequency of Infection with the Tubercle Bacillus in Childhood, Am. J. Dis. Child. **9**:478 (June) 1915.

Roentgen-Ray Examination: A characteristic triangular shadow is to be considered presumptive evidence of this form of tuberculosis.

Lung Puncture: The method of puncture recommended is to use a fairly large needle with a little sterile water in the needle or syringe. Introduce the needle in several directions and aspirate. When it is withdrawn empty the contents of the needle into a sterile test tube. The material thus withdrawn is divided into several portions and examined for the presence of tubercle bacilli by direct spread, for giant cells, and some of it is injected into a guinea-pig.

Enlarged Supraclavicular Glands: Enlarged glands just above the clavicle on the side of the lesion is another point strongly suggestive of active tuberculosis.

This type of tuberculosis has to be differentiated from the following diseases: unresolved pneumonia, either with or without bronchiectasis, pulmonary abscess and encysted empyema, tracheobronchial adenitis, foreign body in the lung, actinomycosis, neoplasm of the lung and streptothrix infections.

The prognosis of tuberculosis (pulmonary) in children is rather serious. The younger the patient the graver the outlook, yet in this type of tuberculosis, as in tracheobronchial adenitis, the prognosis is favorable. The patients whose cases I am reporting recovered, at least clinically. The patients of Wesler and Bass,[4] which evidently belong to the group, also recovered. Increase in weight, steady diminution in temperature and decrease or entire disappearance of cough, are among the early favorable signs.

The treatment is not different from that generally advised for other forms of pulmonary tuberculosis. It consists in the dietetic and hygienic régime. A change of climate is advisable if circumstances allow it. The child should reside in the country, preferably at a considerable altitude, for a year or more. The open air and heliotherapy recommended by Freeman [12] for other pulmonary conditions is of great value here also. Sleeping outdoors is comparatively simple for a child if an intelligent mother or nurse is in attendance. The diet should be liberal, but great care must be exercised against overfeeding, especially in the younger patients.

REPORT OF CASES

Case 1.—(This case was published incompletely in a previous communication.[13]) B. B., female, 1 year old.

Family History.—Negative.

Previous History.—Normal birth, breast-fed up to 7 months, mixed feeding up to the tenth month, weaned at 10 months. Put on formula of top milk. Did well up to present illness.

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12. Freeman, R. G.: Fresh Air in Pediatric Practice, Am. J. Dis. Child. **12**:590 (Dec.) 1916.
13. Med. Rec. **97**:736, 1920.

Fig. 2.—Case 1. Triangular hilus infiltration with the apex extending along the interlobar fissure.

Fig. 3.—Case 1. The hilus infiltration is less definitely outlined than in Figure 2.

Present Illness.—Became ill with a temperature of 102 F., vomited twice at onset; was treated for influenza for two days before I saw her.

Physical Examination.—On examination, I found a fairly well nourished child, not perceptibly prostrated; temperature 103.5 F., fairly rapid pulse; respiration about 30 and acid breath. The skin and glands were negative, as were the mucous membranes; no catarrhal symptoms. The rest of the examination was negative, except for a palpable liver and spleen.

Diagnosis.—A diagnosis of acidosis was made, and the child was treated accordingly. The irregular fever, however, continued for over a month, uninfluenced by treatment. The course of the fever is interesting. It would remit several times during the twenty-four hours and was often highest in the morning and after sleep. The child perspired rather freely. During this period the child never vomited again, had no diarrhea, took its food fairly well and slept normally. The child was examined by several consultants and nothing characteristic was found. I had noticed slight dyspnea several times, but paid no particular attention to it.

Laboratory Examinations.—Several blood examinations showed a high leukocytosis, from 24,300 to 31,000, with from 60 to 65 per cent. polymorphonuclears. Blood and urine cultures were negative.

Date	Leukocytes,	Polymorphonuclears, per Cent.	Lymphocytes, per Cent.	Eosinophils, per Cent.	Mononuclears and Transitionals, per Cent.
Nov. 26	24,600	60	39	1	—
Dec. 4	27,000	57	40	3	—
Dec. 8	34,000	63	35	2	—
Dec. 17	31,000	61	38	1	—
Dec. 24	23,000	54	40	2	4
Feb. 4	26,000	64	30	—	6
Mar. 15	39,000	71	29	—	—
April 4	28,000	69	28	1	2
Jan. 29	29,000	67	33	—	—

Clinical Course.—At the end of about thirty-two days the temperature came down by lysis and remained about normal for several weeks, when it mounted again. About this time the dyspnea became more marked, especially on exertion. This dyspnea was expiratory and was suggestive of pressure behind the pharynx. A search for retropharyngeal suppuration was negative. Diminished breathing over the right lobe posteriorly and slight impairment of resonance was also noticed at the same time.

In the meantime pus was found in the urine and our attention was called to the possibility of latent pyelitis being responsible for the entire clinical picture. Clearing up of the pyuria was not associated with disappearance of the other symptoms, but the diminished breathing and resonance became somewhat more pronounced and the child was then fluoroscoped and radiographed. The roentgenograms showed a triangular area (Figs. 2, 3, 4, 5, 6 and 7), the true nature of which was not then detected.

The diagnosis (roentgenographic) at that time was multiple abscesses or encysted empyema and operation was advised. Chest puncture, however, failed to locate the pus, and the material obtained was injected into a guinea-pig. A von Pirquet test was made about this time and proved strongly positive. Before the guinea-pig could be killed, tubercle bacilli were found in the sputum after more than twenty examinations were made. Two weeks later the guinea-pig showed tuberculosis.

We were reluctant to consider this case tuberculous because of the blood count, which persistently showed a high leukocytosis, and

Fig. 4.—Case 1. Several weeks later, the process apparently was extending.

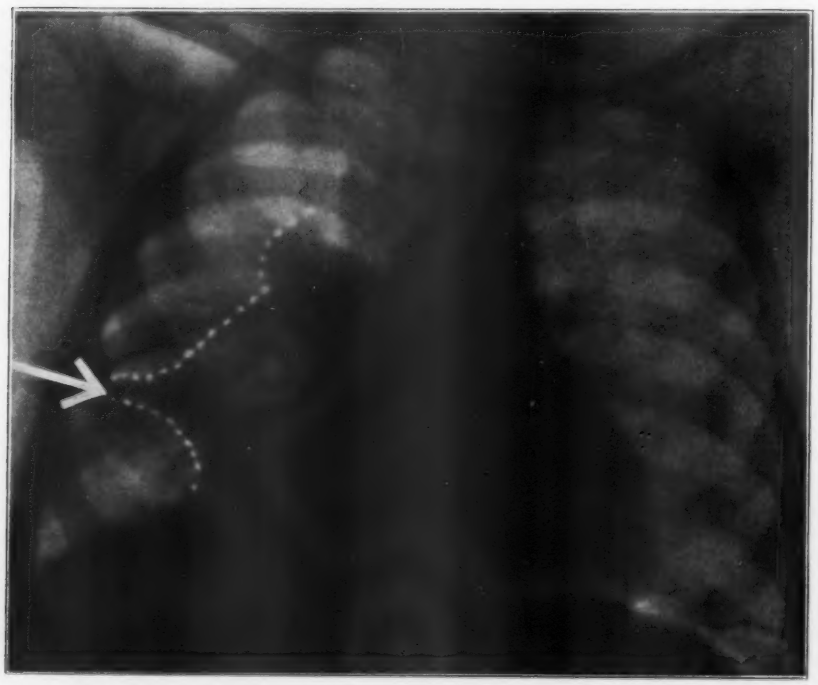

Fig. 5.—Case 1. The process is seen extending along the interlobar fissure. The arrow indicates the presence of free air.

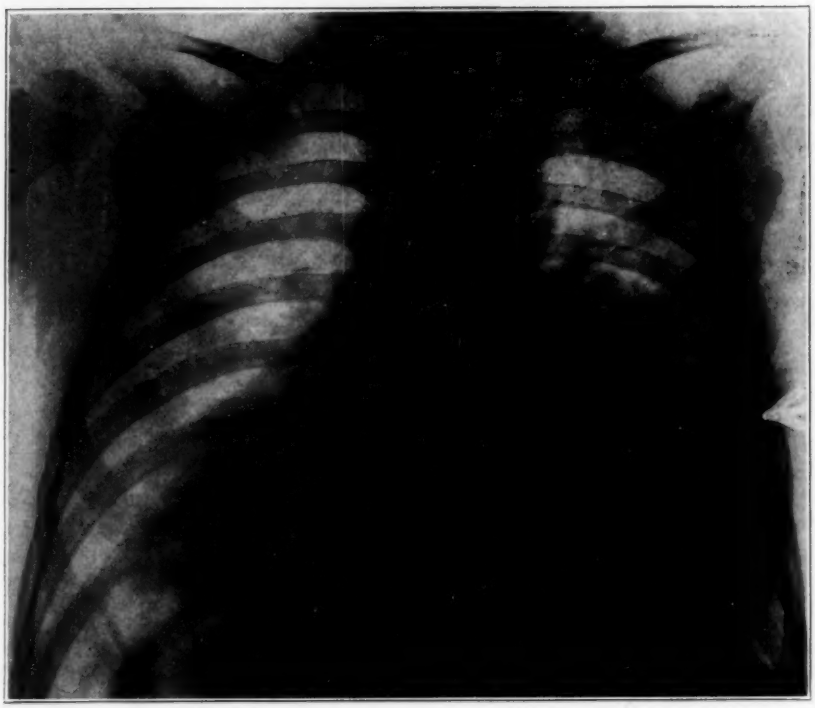

Fig. 6.—Case 1. The process is seen extending along the interlobar fissure.

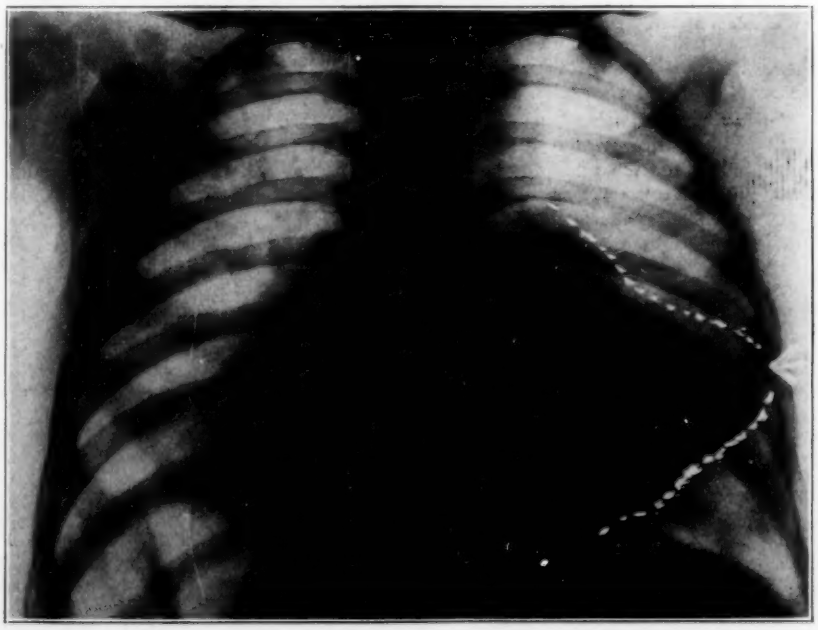

Fig. 7.—Case 1. After a short stay of the patient in the country, the shadow is less dense.

the relative freedom of the upper part of the lung from all evidence of infiltration. The sputum examination and the results of the guinea-pig inoculation definitely established the diagnosis.

After the diagnosis was established, the child was sent to the country and began to improve almost immediately so that now, about a year and a half after the first onset of illness, the child is apparently almost entirely well.

CASE 2.—H. C., male, aged 17 months.

Family History.—One brother died of meningitis (?).

Previous History.—Normal birth, fourth in the family, breast-fed up to 11½ months, no other illnesses. Was told he had enlarged tonsils and adenoids.

Present Illness.—Became ill about June, 1919, with fever, which, according to mother's statement, would come and go. The child was seen by several physicians within the first four weeks of its illness and various diagnoses were made. The family at first did not think that the child's condition was serious, but they became worried after the fever had lasted about a month. While the child had fever almost every day it would still play and would not stay in bed. The mother did not know how high the fever was. When I first saw the patient he had grown perceptibly worse. He had begun to sweat more or less profusely, especially after sleep, and had occasional attacks of hoarseness. No cough was noted previous to this time.

Physical Examination.—Patient was a fairly well nourished child, but slightly prostrated; skin and mucous membranes negative; temperature 103.2 F., pulse 136, respirations 28; head somewhat square-shaped, fontanel open; palpable cervical lymph glands; two very small lymph nodes in right supraclavicular fossa. Chest shows a slight rachitic rosary; moderate dulness over lower lobe posteriorly, except at the very base; relative dulness in right axilla, diminished breathing in axilla, distant bronchovesicular breathing posteriorly, a few fine crepitant râles in the axilla and posteriorly just below the angle of the scapula. The rest of the examination is negative.

Laboratory Examination.—The urine was negative. The sputum, which was obtained by tickling the larynx and catching the coughed-up material on sterile gauze, was negative on three occasions. The blood count was 16,400 leukocytes, with 65 per cent. polymorphonuclears. A chest puncture yielded no fluid and some of the material withdrawn, which consisted of blood stained detritus, was injected into a guinea-pig. Some of this material showed tubercle bacilli by direct spread examination.

The roentgenograms were almost identical with those of Case 1, i. e., the lesion was on the right side, triangular in outline, irregular in density, with a tendency to follow interlobar fissure (Figs. 8, 9, 10 and 11). The roentgenologist made a diagnosis of interstitial pneumonia, probably caused by a foreign body and advised a bronchoscopic examination which, of course, was not done. Subsequently, tubercle bacilli were also found in the sputum. The leukocyte count remained between 16,000 and 21,000.

SUMMARY

1. Extensive tuberculous lesions about the hilus may occur in infants and young children which pursue a rather chronic course.

2. Recovery probably takes place in the majority of these cases even in children under 2 years of age.

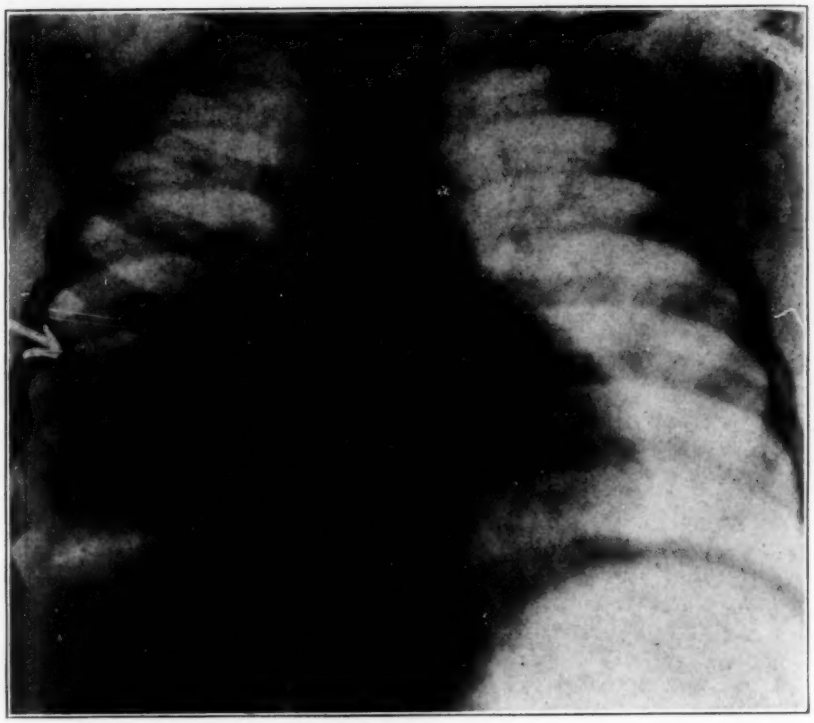

Figure 8

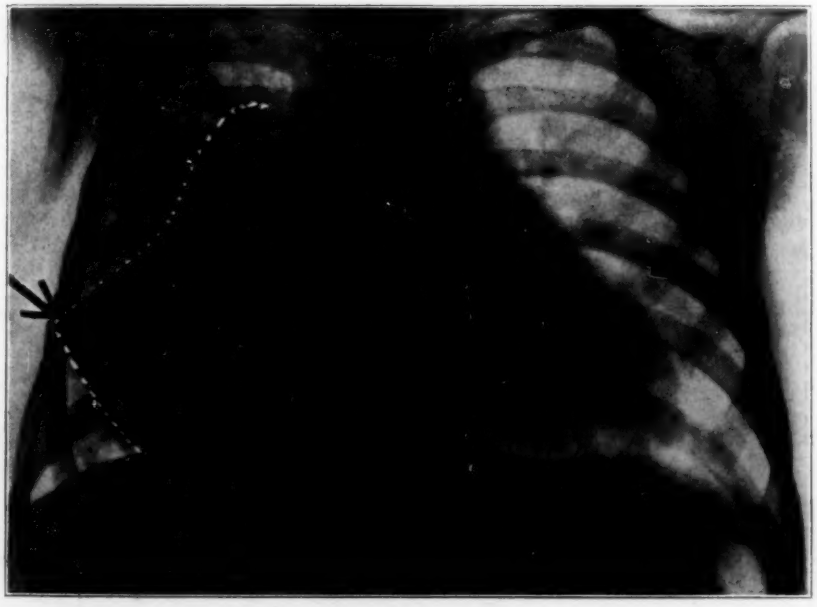

Figure 9

Figs. 8 and 9.—Case 2. Characteristic triangular outline, base toward hilus.

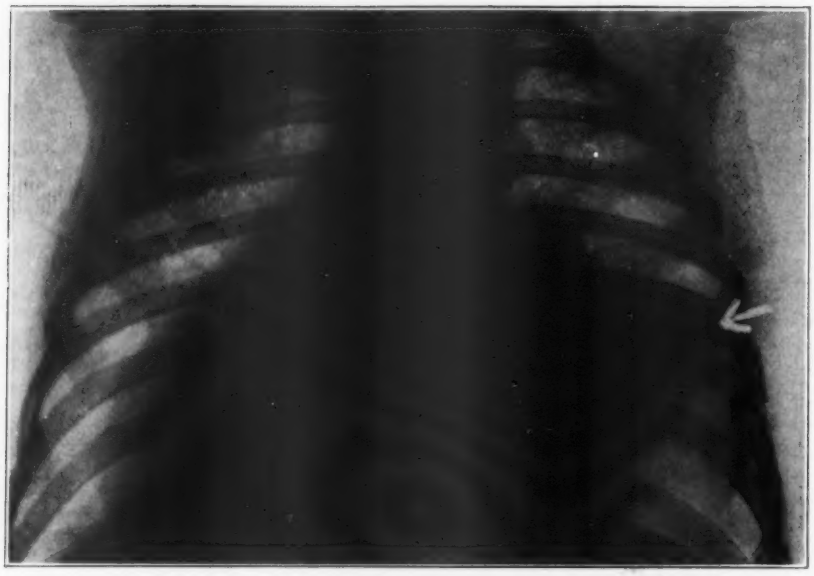

Figure 10

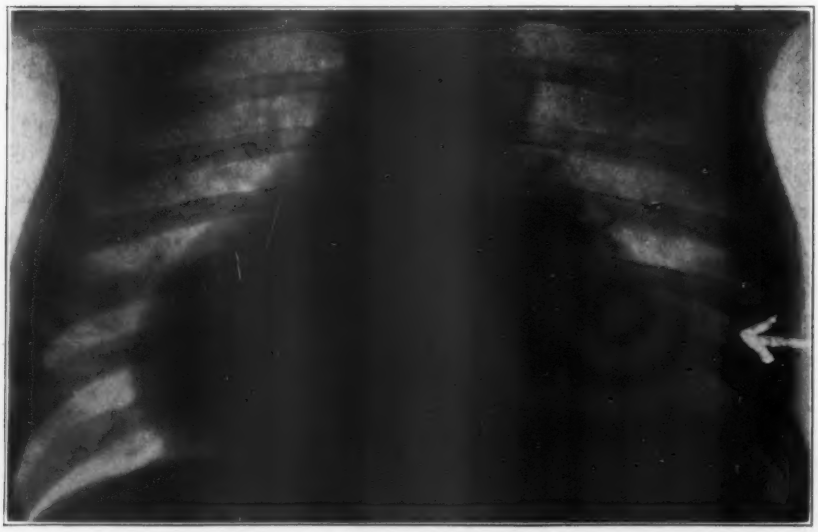

Figure 11

Figs. 10 and 11.—More extensive involvement with irregular density at a time when there began to be clinical improvement.

3. The onset in this type of pulmonary tuberculosis is more or less gradual and there may be no lung signs until after the disease has lasted for some time.

4. Irregular fever, sweating, expiratory obstruction, diminished breathing, with impaired resonance, a positive von Pirquet and a characteristic roentgen-ray picture, are among the earlier manifestations.

5. Enlargement of the supraclavicular lymph nodes, positive results from guinea-pig inoculation of material from lung puncture or of sputum, and the presence of tubercle bacilli in the sputum may be found later in the course of the disease.

6. Given an infant or child with prolonged irregular fever and sweating, showing a positive von Pirquet, this form of tuberculosis should be suspected and its further early manifestations sought for.

COMPLEMENT FIXATION FOR TUBERCULOSIS IN CHILDREN *

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The complement fixation test in tuberculosis has become so well known through a number of recent articles on the subject, and the literature has so often been reviewed that a detailed discussion of previous work is unnecessary. All workers have not been able to secure good results with the test and there has been some lack of conformity between the results of the fixation tests and the clinical diagnoses. It may be mentioned, however, that although different preparations of antigen have been used those investigators whose interest in the reaction has led to a considerable experience in performing the tests have obtained the best and most consistent results. The skepticism that exists in some localities regarding the value of the reaction depends to a certain extent on a lack of understanding of the difficulties in securing a close agreement between the fixation tests and the clinical examination.

Probably several factors have contributed to the inability of all workers with the test to obtain uniform results. One of these is the lack of a uniform technic in performing the test. All tubercle antigens are not equally potent in the reaction, and even two antigens made in the same manner may vary considerably. In addition, there is a very marked difference in the concentration of the fixing antibodies in the blood of different individuals so that while one patient's serum may give a positive fixation in 0.002 c.c., another will give fixation with 0.2 c.c. and not with a less amount, and in a third the concentration of fixing antibodies is so slight that even 0.2 c.c.—the largest amount used in routine tests—contains too little to give a positive result.

The presence of complement fixing antibodies in the blood must depend on the existence in the body of some pathologically active focus of tuberculosis, since the absorption of antigen from such a focus is necessary for the formation of such an antibody. If this lesion is large enough and if there is a considerable absorption from it, there may be definite clinical signs and symptoms. On the other hand, it takes only a slight acquaintance with the necropsy room to realize how frequently small active tuberculous foci, or even rather

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* From the Department of Pediatrics, Washington University, and the St. Louis Children's Hospital.

severe infection may be found without having caused clinical manifestations during life. In such individuals, the necessary mechanism existed for the production of complement fixing antibodies in the circulating blood, even though the patients were considered clinically free from the disease. There is, therefore, some difficulty in harmonizing the results of a series of fixation tests with clinical findings, on account of the not infrequent absence of sufficient clinical evidence to arrive at an exact diagnosis.

The attempt to secure an exact agreement between the results of the complement fixation test and patients with clinical signs of tuberculosis, even with a standardized method, would seem foredoomed to failure for two reasons. First, on account of the lack of sufficient fixing bodies in the blood of certain patients with undoubted active tuberculosis and second, because of the impossibility of recognition by present diagnostic methods of small pathologically active tuberculous foci in some individuals without clinical evidence of the disease. That certain workers, after a considerable experience, have been able to secure an agreement between the test and the clinical diagnosis in from 75 to 90 per cent. of cases seems rather to indicate that under proper conditions the test may be of considerable aid in diagnosis. If others have obtained somewhat less encouraging results, the explanation may lie in one of the factors mentioned above.

Although a considerable number of investigators have reported the results of the complement fixation test in tuberculosis, very few have been interested in making group studies in children. These have included a relatively small number of cases and have given almost negative results. Bauer [1] (1909) examined twenty-one cases of tuberculosis including fifteen infants under 2 years and six children from 8 to 10 years old, with forty nontuberculous children having syphilis, pneumonia, etc. All these gave negative reactions with tuberculin antigen. Certain of the patients were treated with injections of tuberculin, and in all cases so treated, the reaction became positive. Fua and Koch [2] also using tuberculin as antigen tested two series of cases of tuberculous children. The first group of twenty-seven patients, ranging in age from 5 months to 13½ years, untreated by tuberculin, all gave negative results except six, which gave a very weak fixation, but not strong enough to be considered positive by the authors. In the second series, fourteen of forty-one children, aged from 4½ months to 14 years, who had had from two to four doses of tuberculin,

1. Bauer: Komplementablenkung bei tuberculösen Kindern, Verhandl. d. Gesellsch. f. Kinderh. **25**:106, 1909.

2. Fua, R., and Koch, H.: Zur Kenntnis der mit Tuberkulin komplementbindenden Stoffe im Serum tuberculöser Kinder. Beitr. z. klin. d. Tuberk. **14**:79, 1909.

gave positive reactions. Heiman,[3] using Miller's antigen of whole tubercle bacilli in salt solution and Petroff's glycerin-potato-broth filtrate antigen, tested fifty children aged from 6 months to 12 years. Seventeen with various forms of tuberculosis gave two positive reactions, five probably tuberculous cases were all negative, and twenty-eight nontuberculous infants and children gave three positive reactions.

The present paper gives the results of the examination of a large number of serums from infants and children by the complement fixation test using an antigen made from human tubercle bacilli. The patients were from the Pediatric Clinic of the Washington University and from the wards of the St. Louis Children's Hospital. The test was made in general as a routine procedure during a period of two years, although for various reasons many children seen during that period escaped the examination. There was no selection of cases but probably more effort was made to include all children with tuberculosis or suspected tuberculosis. It is only by the use of the test in a large number of unselected cases, together with a careful examination of the material, that any conclusions regarding its value may be made. In this series, a large percentage of the cases were subjected to a rather close examination for evidence of tuberculous infection. A certain proportion of clinic cases, as, for example, healthy infants whose feeding was being supervised, children without history of association with tuberculosis who came for relatively trivial complaints or for health certificates, were given only a general physical examination and no skin tests were done. In some cases, children failed to return for the reading of the tuberculin reactions. On the other hand, many children with only suspicious clinical findings were sent for flat or stereoscopic chest plates, had one or more von Pirquet or intradermal tuberculin tests done, and daily temperature observations were made by the mother. Occasionally, they were admitted to the hospital for more careful study. In every case a clinical diagnosis was made without reference to the result of the fixation test. In all 1,855 fixation tests were done on 1,556 children, and it is believed that the series studied is sufficiently large to justify conclusions from the results obtained.

METHODS

The antigen employed consisted of a dried, powdered alcoholic precipitate of human tubercle bacilli grown on Dorset's egg medium, prepared as described previously,[4] and used in a salt solution emulsion of one mg. of the powder to one c.c. The antigenic dose was

3. Heiman, H.: The Complement Fixation Test for Tuberculosis in Infancy and Childhood, Arch. Pediat. **36**:32 (Jan.) 1919.

4. Cooke, J. V.: Complement Fixation with Acid Fast Bacteria, J. Infect. Dis. **25**:452 (Dec.) 1919.

0.1 c.c. Antigens made from different strains of tubercle bacilli vary considerably in their antigenic and anticomplementary properties and it is sometimes necessary to examine antigens made from several different cultures before securing a satisfactory wide range preparation. In my experience strains that have been cultured for some time are better than freshly isolated ones, but this may not be constant. Two antigens were used in a large number of tests and but little difference was noted.

The hemolytic system used in the tests was 0.5 c.c. of a 1 per cent. sheep cell suspension, sensitized with two units of rabbit antisheep serum of high titer, and two units of complement (1 c.c. of 1:100 dilution of guinea-pig serum).

The patient's serum was inactivated and used in amounts of 0.2, 0.1 and 0.05 c.c. Two additional tubes of 0.2 c.c. each were tested with simple alcoholic and cholesterolized Wassermann antigens and a control of 0.2 c.c. of serum without antigen was always included. The technic of the tests has been previously described [4] in some detail and will only be summarized here. The tubes with serum, antigen and complement were made up to 1.8 c.c. with salt solution, incubated one hour in the water bath at 37 C., the cells (0.5 c.c.) sensitized with two units (0.2 c.c.) of hemolysin added, and reincubated 30 minutes longer. Readings were made after standing over night in the ice box. Only complete inhibition with 0.2 c.c. of serum or less was considered positive.

TABLE 1.—AGE, SKIN TUBERCULIN REACTIONS, AND COMPLEMENT FIXATION RESULTS IN ALL CHILDREN STUDIED

Age in Years	Skin Tuberculin Test Negative		Skin Tuberculin Test Not Done		Skin Tuberculin Test Positive	
	Total Number	Fixation Positive	Total Number	Fixation Positive	Total Number	Fixation Positive
0- 1	48	1	61	2	11	0
1- 2	50	1	26	0	20	8
2- 4	73	4	60	4	44	17
4- 6	84	5	63	1	48	21
6- 9	160	17	124	12	113	53
9-12	120	13	105	14	102	50
12-15	95	7	82	16	66	31
Total	630	48 7.6%	522	49 9.6%	404	180 44.4%

In order to illustrate the ages of the children examined and the relation of the tuberculin skin test to the fixation reaction, the entire series is tabulated in Table 1. It will be seen that a skin test was done in about two-thirds of the cases. Most of these tests were made by the von Pirquet method, but in a considerable number an intracutaneous injection of 0.1 mg. of old tuberculin was done. Not infrequently the intradermal test was positive after a von Pirquet

test had been negative in the same child. This observation has been made by others and is probably due to the greater certainty of a successful tuberculin inoculation by the intradermal method. In this series the intradermal test has proved much more reliable than the von Pirquet, although in many cases only the latter was done. Somewhat less than half the children with positive skin tests gave positive fixations, while of those with negative skin tests 7.6 per cent. gave positive fixations. The latter group, however, included cases of proved tuberculosis with negative skin reactions and other nonspecific reactions to be mentioned later, so that this figure is somewhat misleading. Approximately 100 children in each year from the first to the fifteenth were examined so that the distribution of the tests is fairly uniform so far as age is concerned.

TABLE 2.—Results of Complement Fixation Reactions in Children with Tuberculosis

Age, Years	Manifest Tuberculosis			Masked Tuberculosis			Suspected Tuberculosis		Healed Tuberculosis	
	Number Tested	Fixation Positive	Per Cent. Positive	Number Tested	Fixation Positive	Per Cent. Positive	Number Tested	Fixation Positive	Number Tested	Fixation Positive
0–1	12	0	0	—	—	—	1	0	—	—
1–2	16	7	44	5	2	40	1	0	—	—
2–4	26	10	38	10	5	50	3	2	—	—
4–6	16	9	56	19	12	63	1	0	2	0
6–9	18	15	83	45	33	73	4	2	8	0
9–12	17	14	82	31	23	74	7	5	6	2
12–15	11	9	82	21	20	95	7	4	4	0
Total	116	64	55	131	95	73	24	13	20	2
4–15	62	47	76	116	88	76				

In Table 2 the results of the fixation tests in children with tuberculosis are summarized. By a careful clinical study of each case, these children have been separated into four groups called manifest, masked, suspected and healed tuberculosis, respectively.

The first group of children with manifest tuberculosis includes the cases in which there was no doubt concerning the diagnosis of an active tuberculous process at the time of examination. In addition to a typical clinical picture, the diagnosis was confirmed in each instance by necropsy, demonstration of the organisms or, especially in the bone cases, convincing and characteristic roentgenograms. There were sixty-six children with generalized tuberculosis, meningitis or pulmonary involvement, and fifty with lymph node, bone or joint tuberculosis. Because of the close agreement in the proportion of positive fixations found in these two groups of children they were tabulated together. In infants under 1 year of age a positive skin tuberculin reaction alone was considered sufficient proof of an active lesion. The results in the group of manifest tuberculosis cases show

a very definite relation to the age. During the first year no positive fixation reactions occurred, while from the second to the fourth years about 40 per cent. of the children reacted positively to the test. From the fourth to the sixth year this percentage increased to 56 and above six years over 80 per cent. showed positive reactions. The small proportion of positive results in the early years of life makes the total percentage of positive reactions somewhat low (55 per cent.), although if the group from four to fifteen years only is considered, the percentage of positive cases is increased to 76. The substances in the blood which give the complement fixation reaction appear distinct from those antibodies which cause the skin tuberculin reaction. This is shown by the fact that of the eight cases of manifest tuberculosis which gave negative skin tests four gave positive fixation reactions and of the four giving negative reactions, two patients were under 2 years of age and two were 4 years old. It has been mentioned that children of these ages gave positive fixations in less than half the instances. These were children with miliary tuberculosis or tuberculous meningitis and in these severe infections such a suppression of the skin reaction is not unusual.

The cases of masked tuberculosis were of particular interest. In the course of the study increasing numbers of positive fixations were noted in children who had no obvious tuberculosis. On closer examination, however, these children all showed certain of the symptoms that frequently accompany tuberculosis, such as malnutrition, asthenia, slight fever, anemia, loss of weight, etc., with positive tuberculin skin tests. Accordingly, a special study was made of all children who exhibited one or more of such clinical signs. Evidence of tuberculosis was sought by repeated careful physical examination and in most cases roentgenography of the chest. A more detailed report of this group appears elsewhere,[5] and will merely be summarized. The characteristic clinical picture includes the following: A history of frequent coughs and colds, attacks of unexplained fever often with afternoon elevations, anorexia, loss of weight and asthenia. There may or may not be known exposure to tuberculosis. On physical examination there is more or less malnutrition, occasionally anemia, and chest signs referable to enlarged tracheobronchial lymph glands. The von Pirquet or intradermal tuberculin skin test is positive and in certain instances there is phlyctenular disease of the eye or skin tuberculids. The diagnosis of masked tuberculosis in cases of this group was made from clinical examination alone and did not rest on any one of the above mentioned points but on a review of all the findings. It is difficult to prove that these children have active tuberculosis but from the studies made it seems very probable that each

5. Cooke, J. V., and Hempelmann, T. C.: Masked Juvenile Tuberculosis, Am. Rev. Tuberc. **4**:660, 1920.

of them harbors a tuberculous focus that is pathologically active even though this lesion is not large enough to cause the marked clinical signs and symptoms that we find in more easily recognized cases of tuberculosis in childhood. The complement fixation tests on these children support the view that the process is an active one since the number of positive results in children of the different ages parallels closely those found in the manifest tuberculosis group. The same increase in positive reactions is found as the age advances. The higher percentage (73) for the whole group of masked tuberculosis is due to the relatively small number of younger children studied. If only those over 4 years old are considered, the percentage of positive fixations is the same for the manifest tuberculosis group as for those with masked tuberculosis.

The concentration of the fixing substances in the blood varies considerably in different children as it does in adults. Of the 159 cases of manifest and masked tuberculosis that gave positive fixations, twenty-seven did not react with less than 0.2 c.c. of serum, fifty-five had a minimal fixing dose of 0.1 c.c., and seventy-seven gave fixation in amounts of 0.05 c.c. or less. A few of these latter strongly positive serums upon titration gave fixation with 0.004 c.c. This concentration of fixing antibody in the blood has no demonstrable relation to the type or severity of the disease. Such marked differences in antibody concentration as have been shown to occur in the serums studied suggest the most probable explanation for the negative fixation reaction found in a certain number of cases of active tuberculosis. It would be unusual if some cases did not show an antibody content so low that 0.2 c.c. of serum contains too little to be recognized in the test. For several reasons, however, the routine use of larger amounts of serum is impracticable.

In a certain number of instances, the presence of tuberculosis was suspected from certain findings but the examinations were incomplete. These cases could be included neither with the tuberculosis groups nor with those free from tuberculosis so they were classified separately and called "suspected tuberculosis." About half of this small group showed positive fixations.

It was possible to examine only twenty cases of healed tuberculosis. These children had all been observed during an active tuberculosis some years previously. Both pulmonary and bone tuberculosis cases were represented and all had been free from any sign of the disease for from two to six years. Only two of this group gave positive complement fixation tests. Since these children were all over 4 years of age, the results give additional evidence of the association of active tuberculosis with a positive fixation reaction.

Before taking up the control group of children without clinical tuberculosis, two conditions should be mentioned in which nonspecific fixation reactions are found. These are hereditary syphilis and diphtheria. In Table 3 are given the results of the tests on children with these two diseases in which it will be seen that almost one-third of the cases have reacted to the complement fixation test for tuberculosis. The syphilis cases all showed a strongly positive Wassermann reaction although fifteen others which had been treated until the Wassermann was negative failed to give a positive fixation test for tuberculosis. Some of the older children had positive tuberculin skin tests but none had demonstrable evidence of tuberculosis. There is no such relation of positive fixation to age as is found in the tuberculosis cases and several children in the first year of life gave positive fixation reactions, a finding quite at variance with the results in tuberculosis. From these observations it seems evident that children with hereditary syphilis and a strongly positive Wassermann reaction may give a positive complement fixation test for tuberculosis in the absence of any tuberculosis in such children. The explanation of this nonspecific fixation is not clear but it seems likely that in children with a high concentration of syphilitic antibodies in the blood, the tubercle antigen has an action similar to the other nonspecific lipoid antigens used in the Wassermann test. The antibodies giving the Wassermann reaction are usually present in considerably higher concentration in children with hereditary syphilis than in adults with the acquired form of the disease. This has been determined by titrating the minimal fixing dose of serum from a number of cases.

TABLE 3.—RESULTS OF COMPLEMENT FIXATION FOR TUBERCULOSIS IN CONGENITAL SYPHILIS AND DIPHTHERIA

Age in Years	Syphilis		Diphtheria	
	Number Tested	Fixation Positive	Number Tested	Fixation Positive
0- 1	14	3	..	..
1- 2	9	0	..	..
2- 4	9	2	8	2
4- 6	7	2	10	3
6- 9	11	3	20	6
9-12	11	7	8	4
12-15	14	4	3	0
Total	75	21 28%	49	15 30.6%

The relatively high percentage of diphtheria cases giving a positive fixation test for tuberculosis was quite unexpected. These tests were made on children after the acute symptoms of the disease had subsided and on others suffering from postdiphtheritic polyneuritis. All cases had negative skin tuberculin tests, except seven which

included only one of those giving positive fixations. In none of the group could any evidence of tuberculosis be found so that the negative reactions appear definitely nonspecific. That the presence of such fixing bodies in the blood is probably transient is indicated by observations made on two children who had negative fixations before and six months after the diphtheria with strongly positive reactions during the attack. All patients had been given antitoxin and these children were the only ones studied in whom a foreign protein had been injected. In a previous paper[4] it was shown that highly immune serums may give a nonspecific fixation with other antigens if relatively large amounts (0.1 c.c.) of serum are used. Whether the nonspecific fixation noted after diphtheria is in any manner associated with the serum injection or whether it is due to a high concentration of specific immune substances of the diphtheritic infection, has not been determined.

TABLE 4.—COMPLEMENT FIXATION TESTS FOR TUBERCULOSIS IN CHILDREN WITH NO CLINICAL TUBERCULOSIS AND WITH NEGATIVE WASSERMANN REACTIONS (NO DIPHTHERIA INCLUDED)

Age in Years	Skin Tuberculin Test Negative		Skin Tuberculin Test Not Done		Skin Tuberculin Test Positive	
	Total Number	Fixation Positive	Total Number	Fixation Positive	Total Number	Fixation Positive
0- 1	42	..	51	..	...	...
1- 2	47	..	17	..	1	...
2- 4	63	1	51	2	7	1
4- 6	68	1	60	..	12	...
6- 9	139	7	112	8	40	8
9-12	108	5	96	9	41	8
12-15	88	5	68	8	27	4
Total	556	19 3.4%	457	27 5.9%	128	21 16.4%

Table 4 shows the results of the complement fixation test for tuberculosis in children with no evidence of clinical tuberculosis. No cases of syphilis with positive Wassermann reactions are included and no cases of diphtheria or postdiphtheritic paralysis. The group is composed of normal children and those with the common ailments of infancy and childhood. In infants, the various nutritional disorders, rickets, tetany, scurvy, congenital heart disease, bronchitis, pneumonia, otitis, stomatitis, iliocolitis, poliomyelitis, pyelitis, meningitis and sepsis formed the bulk of the cases. Among the older children groups of cases were examined with the infectious exanthemas, typhoid fever, malaria, pertussis, rheumatic fever, influenza, pneumonia, meningitis, mumps, osteomyelitis, encephalitis and other acute infections, as well as chronic diseases such as nephritis, cardiac decompensation, leukemia, tumors, Banti's disease, epilepsy, diabetes mellitus, diabetes insipidus, chronic arthritis, and in fact all the various

medical and surgical conditions seen in a general pediatric service during a period of two years. In none of these diseases was there found any tendency to react positively to the fixation test. As may be seen from Table 4, a certain number of children, however, did give positive reactions. A rather small percentage (3.4) of those with negative skin tuberculin tests gave positive fixations. The diagnosis in these nineteen cases may be of some interest.

There were four cases of chronic pneumonia, three of chronic cervical adenitis, three of chronic bronchitis and malnutrition, two of mental deficiency and one each of pneumonia, typhoid fever, malaria, chronic endocarditis, chronic nephritis, hypertrophied tonsils and simple malnutrition. In those cases with positive fixations in which the skin tuberculin tests were positive or not performed, it is possible that some focus of active tuberculosis was present although none was detected. The obvious difficulties in recognizing clinically every such case needs no comment, and it is of interest in this connection that of the children without clinical evidence of tuberculosis, five times as many with positive skin tuberculin tests gave positive fixation reactions as those with negative skin tests.

DISCUSSION

Several features of some interest have been observed in the series of complement fixation tests for tuberculosis. In manifest tuberculosis, there has been a striking relation between the age of the child and a positive fixation reaction. More than 80 per cent. of those over 6 years of age gave positive reactions, a proportion similar to that found in adults,[4] while none in the first year reacted positively to the test. From the second to the sixth year gradually increasing numbers of children develop fixing antibodies. There are two possible factors in the failure of infants and young children to develop complement-fixing substances in the blood. The duration of the infection may influence their formation and the younger children may have had the infection too short a time for the development of such antibodies. This explanation seems less likely than that young animals may form antibodies much less readily than older ones. The Wassermann reaction in syphilis is not a specific fixation, and consequently there is no true analogy, but even here infants with hereditary syphilis may give a negative Wassermann at birth and not develop a positive one until several months later. The absence of fixing bodies in tuberculosis of infants and in a considerable proportion of younger children may have some relation to the very rapid spread of the disease at this time of life which is commonly observed, since the inability to form fixing antibodies may be associated with a lack of power to form other protective antibodies.

The absence of complement-fixing antibodies in young children, however, has little importance in the question of diagnosis since it is at this age that the tuberculin skin tests are of greatest value in calling attention to an active infection. In older children, on the other hand, the skin tests do not always indicate the presence of an active tuberculous process, and it is here that the complement fixation test is of particular value, because of the high proportion of tuberculous children who give a positive reaction.

In a large number of children the tuberculous infection, usually of the tracheobronchial glands, is slight in extent and the process is masked by the relatively insignificant clinical signs that are commonly present. There seems little doubt, however, that in these cases the infection is pathologically active since there is sufficient continuous absorption from the tuberculous focus to produce complement-fixing antibodies. The children of this masked tuberculosis group give positive complement fixation reactions in the same proportion as those with manifest tuberculosis. The test is consequently of great aid in calling attention to this rather common and frequently overlooked type of tuberculosis in children. Additional evidence that a positive fixation test is associated with a pathological activity of the tuberculous process if furnished by the relatively small number of children with clinically healed tuberculosis who give positive reactions.

Certain nonspecific reactions may occur in children with congenital syphilis and a strongly positive Wassermann test, and also in cases of diphtheria for several months after the acute attack. This should be borne in mind to prevent misinterpretation of positive fixation reactions in these conditions. In more than one thousand other cases in which no clinical tuberculosis could be demonstrated, positive fixation reactions were found in less than 5 per cent. The great difficulty in absolutely excluding tuberculous infection by present diagnostic methods suggests that some of these apparent "false positives" may not be quite free of the disease.

The test has proved of considerable value not only in calling attention to cases of tuberculosis without well defined clinical signs, but in making a decision regarding the presence of active tuberculous foci in children exposed to the disease and also in following the course of a healing lesion. The complement fixation reaction, however, must not be considered a relatively easy and infallible method of diagnosing an active tuberculous process. It is of most value when used as an aid to a careful and complete physical examination of the patient. The results show that a positive fixation reaction is associated in a large majority of cases with a tuberculous lesion that is pathologically if not clinically active, and consequently any patient giving a positive reaction should not be considered free from active tuberculosis without a thorough study.

PRECIPITINS TO EGG WHITE IN THE URINE OF NEW-BORN INFANTS*

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In 1904, Ganghofer and Langer [1] carried out some experiments on animals to test the permeability of the intestinal wall to foreign albumin. Their examinations consisted of precipitin reactions on the blood of new-born animals. They found that in young dogs or other animals previous to the sixth day of life, the precipitin reactions to foreign albumin were positive although the quantity of albumin consumed was very small. Their experiments were carried out on dogs, cats, rabbits and kids.

In 1913, Lust [2] attempted to determine the presence of egg white in the urine of infants. For this purpose he used precipitin serum, which gave the reaction in dilution of 1 : 100,000; oftentimes of 1 : 1,000,000. He used egg albumin because it was much easier to recognize by the precipitin reaction. In his first series of ten infants suffering from various types of nutritional disturbances, he found that while the precipitin reaction was present in the blood in none of his cases, he was able to obtain four positive results in the urine. Against the objection that egg white may be irritating to the intestinal canal after use in large quantities, he states that for the test of permeability one does not have to take into consideration any slight irritation which may occur from the single ingestion.

In a series of twelve normal infants which he examined, he was able to obtain no reactions, even though the dosage of the egg was increased up to 55 and 60 gm. Among nine infants with acute dyspepsia, however, treated in the same manner, there were three positive reactions. In seven cases of severe dyspepsia, intoxication and colitis, in all but one there were definite reactions. Age seemed to play no rôle, nor did the quantity, the dose of the egg white being at least ten times less than to the normal individual. He thinks, therefore, that the physical processes in the bowel are not dissimilar from those obtained by Mayerhofer and Pribam [3] in their experiments on the intestines of infants dead of acute and of chronic nutritional disturbances.

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1. München. med. Wchnschr. **51**:1497, 1904.
2. Jahrb. f. Kinderh. **77**:243, 383, 1913.
3. Wien. klin. Wchnschr. **22**:875, 1909.

In nineteen cases of chronic nutritional disturbances he was able to recognize egg white in the urine in twelve; the intensity of the reaction, however, was far below that obtained in the acute cases. During the reparative stage there seemed to be a gradual resumption of function on the part of the intestines. It would seem from this that even though the intestinal wall in these cases allows heterologous albumins to pass, no irreparable damage is produced by this. His examinations for cow's milk protein were unsatisfactory. In only one case out of seventeen was it possible to recognize the albumin. Examinations on animals, however, were more successful. Excretion began usually after two or three hours, increased from then on, and went slowly after six or eight hours. In no case was it possible to obtain a reaction after twenty-four hours. The quantity of albumin was never sufficient to be determined chemically.

Hahn [4] confirmed Lust's work, using diphtheria antitoxin. He was not able to obtain any reaction in intestinally healthy infants, but was in those with nutritional disturbances when large quantities of antitoxin were used.

Lawatschek [5] examined by the precipitin reaction the urine of the new-born for egg albumin. He gave at least the white of half an egg at one time; the urine was collected and examined, immediately. In four of twenty-one cases there was a pronounced reaction for egg albumin in the urine (six of the cases were dyspeptic infants). The largest number of reactions occurred on the second, eighth and ninth days. After the tenth day the reactions were weaker. In the older infants his results corresponded very closely to those of Lust.

Hayashi [6] used the precipitin reaction on the urine in testing the permeability of the infant's intestinal wall for egg albumin, and also examined the urine for disaccharids. The reactions were obtained in from two and one-half to eight and one-half hours after ingestion. The youngest child was 1¼ months old, and the ages varied from that up to 12 months. Normal children required from 12 to 30 gm. of egg white per kilogram of body weight.

A second series of eleven cases, of which five were eczemas, the patients being from 2 to 8 months of age, reactions occurred in from two to seven hours and were obtained by using from 12 to 18 gm. In five cases following acute gastro-intestinal disturbances the amount used was from 10 to 12 gm. In a series of sixteen cases in which he tested the permeability, not only of egg albumin but also of cane sugar and milk sugar, he found that the quantity of egg albumin per

4. Jahrb. f. Kinderh. **77**:405, 1913.
5. Prag. med. Wchnschr. **39**:185, 1914.
6. Monatschr. f. Kinderh. **12**:749, 1914.

kilogram of body weight necessary for its recognition in the urine was from 10 to 20 gm., of the cane sugar from 3 to 8 gm., and of the milk sugar from 2 to 8 gm.

Modigliani and Benini [7] examined the blood of infants for precipitin reaction to cow's milk casein. They prepared a rabbit serum for this purpose. Their first series consisted of ten children, aged from 3 to 9 months. There were two positive reactions in the nourishment disturbed infants, one a chronic and the other an acute reaction. In their second series of nineteen children, aged from 4 days to 4 months, they had seven positive and three doubtful reactions. Of the seven positive reactions, four were acute, and three in cases of chronic nutritional disturbances. Of the three doubtful reactions one child was normal, one was suffering with acute, and the third with chronic nutritional disturbance.

In a 4 day old normal infant there was no reaction, and in a 10 day old infant with acute disturbance the reaction was doubtful.

Schloss and Warthin,[8] in examining the gastro-intestinal tract of infants for undigested protein, used egg white for this purpose. The white of one or two eggs was given and the urine collected for six hours thereafter. In fourteen normal infants they obtained two positive results. In seven infants with mild gastro-enteric dyspepsia two showed positive reactions; three out of four children with moderately severe symptoms gave a positive reaction; and six with severe symptoms all showed positive reactions at some time during the disease. In six cases of eczema the results were positive in three.

The present investigations were undertaken in order to determine the permeability of the intestinal tract of the new-born infant to egg albumin. The cases were, so far as possible, routine cases taken from the service at the hospital. They differed in no way from cases of a like sort which we had been observing in the hospital for several years. They were not selected cases. In order that the conditions under which these children lived might show no variation from those which had been observed previously, no special change was made in the routine treatment of the case. The only way in which the care of these infants differed from that of previously observed cases was that the children were given the egg albumin in a manner to be described later and specimens of the urine were collected so far as possible daily. No attempt was made to obtain twenty-four-hour specimens. Single specimens were usually obtained by the night nurse, the so-called morning specimen. The egg white was given in a 2 per cent. solution (10 c.c. to 500 c.c. of water).

7. Policlinico, Sez. Med. **21**:540, 1914.
8. Am. J. Dis. Child. **11**:342 (April) 1916.

TABLE 1.—Results of Examination From First to Thirteenth Day After Feeding Albumin Water

Number	Case No.	Weight	C.c. Albumin Water	Gm. Albumin	Gm. per Kg.	Reaction
1	132446					
	1st day	3,408	56	1.12	0.33	—
	2d day	3,280	32	0.64	0.20	—
	3d day	3,056	32	0.64	0.21	—
	4th day	3,152	96	1.92	0.62	—
	5th day	3,328	44	0.88	0.27	—
	6th day	3,360	112	2.24	0.68	—
	7th day	3,456	80	1.60	0.47	—
	8th day	3,408	96	1.92	0.56	—
	9th day	3,264	104	2.08	0.65	—
	10th day	3,264	52	1.04	0.33	++
2	132531					
	1st day	3,776	32	0.64	0.17	—
	2d day	3,664	56	1.12	0.31	—
	3d day	3,680	96	1.92	0.53	—
	4th day	3,632	56	1.12	0.31	—
	5th day	3,696	64	1.28	0.36	—
	6th day	3,712	64	1.28	0.35	—
	7th day	3,760	56	1.12	0.30	++
	8th day	3,744	24	0.48	0.13	0
	9th day	3,728	48	0.96	0.26	—
	10th day	3,760	50	1.12	0.30	—
3	132532					
	1st day	3,232	32	0.64	0.20	—
	2d day	3,264	80	1.60	0.50	—
	3d day	3,168	128	2.56	0.82	—
	4th day	3,200	80	1.60	0.50	—
	5th day	3,216	64	1.28	0.40	—
	6th day	3,296	120	2.40	0.73	—
	7th day	3,312	112	2.24	0.68	—
	8th day	3,280	68	1.36	0.41	—
	9th day	3,408	128	2.56	0.75	++
	10th day	3,392	64	1.28	0.38	—
4	132631					
	1st day	4,032	48	0.96	0.24	—
	2d day	3,952	56	1.12	0.29	—
	3d day	3,856	104	2.08	0.55	—
	4th day	3,824	96	1.92	0.51	—
	5th day	3,872	88	1.76	0.46	+
	6th day	3,920	48	0.96	0.25	++
	7th day	3,936	56	1.12	0.29	0
	8th day	3,968	80	1.60	0.41	—
	9th day	4,048	80	1.60	0.40	—
	10th day	4,048	—	—	—	—
5	132588					
	1st day	4,096	32	0.64	0.34	—
	2d day	3,968	80	1.60	0.41	—
	3d day	3,888	80	1.60	0.41	—
	4th day	4,000	80	1.60	0.40	—
	5th day	4,016	56	1.12	0.28	0
	6th day	4,064	56	1.12	0.28	0
	7th day	4,112	32	0.64	0.12	—
	8th day	4,144	72	1.44	0.35	0
	9th day	4,176	112	2.24	0.55	±
	10th day	4,144	32	0.64	0.15	—
6	132654					
	1st day	3,680	64	1.28	0.30	—
	2d day	3,536	80	1.60	0.46	—
	3d day	3,376	64	1.28	0.39	—
	4th day	3,340	48	0.96	0.29	++
	5th day	3,472	64	1.28	0.38	+
	6th day	3,552	80	1.60	0.46	+
	7th day	3,568	96	1.92	0.55	0
	8th day	3,632	48	0.96	0.27	0
	9th day	3,696	80	1.60	0.43	0
	10th day	3,792	48	0.96	0.25	++
	11th day	3,584	56	1.12	0.31	+
	12th day	3,760	16	0.32	0.09	0
	13th day	3,744	80	1.60	0.43	+
7	132673					
	1st day	4,656	64	1.28	0.18	—
	2d day	4,496	112	2.24	0.50	—
	3d day	4,400	40	0.80	0.18	—
	4th day	4,432	48	0.96	0.22	—
	5th day	4,496	88	1.76	0.40	0
	6th day	4,544	112	2.24	0.50	0
	7th day	4,528	64	1.28	0.28	0
	8th day	4,496	80	1.60	0.36	±
	9th day	4,560	32	0.64	0.14	++
	10th day	4,560	16	0.32	0.07	—
8	132695					
	1st day	3,504	32	0.64	0.13	—
	2d day	3,248	48	0.96	0.30	0
	3d day	3,216	64	1.28	0.40	0
	4th day	3,248	104	2.08	0.65	0
	5th day	3,248	64	1.28	0.40	+
	6th day	3,296	72	1.44	0.44	+++
	7th day	3,344	48	0.96	0.29	0
	8th day	3,376	48	0.96	0.29	++
	9th day	3,392	32	0.64	0.19	+
9	133056					
	1st day	3,456	0	0.00	—	0
	2d day	3,328	64	1.28	0.39	0
	3d day	3,296	64	1.28	0.40	0
	4th day	3,280	48	0.96	0.30	0
	5th day	3,344	64	1.28	0.39	0
	6th day	3,344	80	1.60	0.50	+
	7th day	3,408	40	0.80	0.24	0
	8th day	3,440	64	1.28	0.38	—
	9th day	3,440	64	1.28	0.38	0
	10th day	3,488	—	—	—	—
10	133161					
	1st day	3,808	16	0.32	0.04	0
	2d day	3,616	32	0.64	0.18	0
	3d day	3,520	40	0.80	0.23	—
	4th day	3,600	28	0.56	0.16	—
	5th day	3,728	64	1.28	0.35	0
	6th day	3,872	56	1.12	0.30	0
	7th day	3,888	32	0.64	0.16	0
	8th day	3,952	52	1.04	0.26	±
	9th day	3,968	88	1.76	0.45	—
	10th day	—	16	0.32	—	0
11	133211					
	1st day	3,696	8	0.16	0.04	—
	2d day	3,636	16	0.32	0.09	—
	3d day	3,424	48	0.96	0.28	—
	4th day	3,392	0	0.00	—	—
	5th day	3,440	48	0.96	0.28	+
	6th day	3,456	40	0.80	0.23	0
	7th day	3,472	68	1.36	0.40	0
	8th day	3,440	64	1.28	0.38	—
	9th day	3,504	48	0.96	0.25	0
	10th day	3,456	56	1.12	0.33	0
	11th day	3,536	16	0.32	0.09	—
12	133254					
	1st day	4,320	8	0.16	0.10	—
	2d day	4,112	64	1.28	0.31	0
	3d day	4,048	32	0.64	0.16	—
	4th day	3,856	96	1.92	0.51	—
	5th day	3,808	104	2.08	0.55	+
	6th day	3,904	80	1.60	0.41	0
	7th day	3,888	136	2.72	0.70	+
	8th day	3,984	64	1.28	0.32	—
	9th day	4,048	128	2.56	0.64	0
	10th day	4,096	168	3.36	0.82	0
	11th day	4,112	96	1.92	0.47	+
	12th day	4,176	160	3.20	0.76	0
	13th day	4,192	16	0.32	0.08	—

TABLE 1.—Results of Examination From First to Thirteenth Day After Feeding Albumin Water.—*Continued*

Number	Case No.	Weight	C.c. Albumin Water	Gm. Albumin	Gm. per Kg.	Reaction
13	133297					
	1st day	3,424	16	0.32	0.10	0
	2d day	3,312	32	0.64	0.19	0
	3d day	3,168	48	0.96	0.31	0
	4th day	3,168	48	0.96	0.31	±
	5th day	3,280	56	1.12	0.38	0
	6th day	3,296	40	0.80	0.24	0
	7th day	3,264	64	1.28	0.40	0
	8th day	3,296	48	0.96	0.28	—
	9th day	3,344	72	1.44	0.44	0
	10th day	3,328	—	—	—	—
14	133324					
	1st day	4,240	0	0.00	—	—
	2d day	4,096	16	0.32	0.08	—
	3d day	3,888	28	0.56	0.14	—
	4th day	3,760	104	2.08	0.56	0
	5th day	3,712	96	1.92	0.52	0
	6th day	3,792	72	1.44	0.40	0
	7th day	3,872	96	1.82	0.51	+
	8th day	3,920	64	1.28	0.33	±
	9th day	3,920	64	1.28	0.33	—
	10th day	3,936	80	1.60	0.41	0
	11th day	3,984	64	1.28	0.30	—
	12th day	3,888	0	0.00	0.00	0
	13th day	3,824	32	0.64	0.17	—
15	132884					
	1st day	3,536	0	0.00	—	0
	2d day	3,456	0	0.00	—	—
	3d day	3,344	56	1.12	0.34	0
	4t hday	3,312	32	0.64	0.19	0
	5th day	3,376	44	0.88	0.27	0
	6th day	3,424	32	0.64	0.19	+
	7th day	3,472	72	1.44	0.34	+
	8th day	3,504	8	0.16	0.05	0
	9th day	3,520	40	0.80	0.23	0
	10th day	3,552	16	0.32	0.09	—
16	132901					
	1st day	3,296	16	0.32	0.10	0
	2d day	3,232	48	0.96	0.30	0
	3d day	3,200	32	0.64	0.20	0
	4th day	3,216	48	0.96	0.30	—
	5th day	3,232	76	1.52	0.47	—
	6th day	3,280	32	0.64	0.19	0
	7th day	3,312	32	0.64	0.19	++
	8th day	3,344	8	0.16	0.05	0
	9th day	3,424	48	0.96	0.28	—
	10th day	3,328	—	—	—	—
17	133157					
	1st day	3,184	16	0.32	0.10	0
	2d day	3,088	8	0.16	0.05	0
	3d day	3,008	32	0.64	0.21	0
	4th day	3,120	16	0.32	0.10	—
	5th day	3,136	48	0.96	0.31	+
	6th day	3,088	64	1.28	0.43	—
	7th day	3,184	64	1.28	0.40	0
	8th day	3,200	48	0.96	0.30	0
	9th day	3,264	48	0.96	0.30	—
	10th day	3,280	48	0.96	0.29	+
18	132653					
	1st day	4,720	16	0.32	0.07	—
	2d day	4,608	64	1.28	0.28	—
	3d day	4,336	72	1.44	0.34	—
	4th day	4,112	96	1.92	0.48	—
	5th day	4,104	144	2.88	0.70	—
	6th day	4,096	80	1.60	0.40	—
	7th day	4,080	64	1.28	0.31	0
	8th day	4,176	76	1.52	0.37	0
	9th day	4,272	32	0.64	0.05	0
	10th day	4,304	32	0.64	0.15	0
	11ht day	4,384	0	0	0	0
	12th day	4,304	24	0.48	0.11	0
	13th day	4,368	24	0.48	0.11	0
19*	132996					
	1st day	3,200	16	0.32	0.10	0
	2d day	2,944	36	0.72	0.24	0
	3d day	2,880	0	0.00	—	0
	4th day	2,912	16	0.32	0.11	0
	5th day	3,072	48	0.96	0.32	0
	6th day	3,152	48	0.96	0.31	0
	7th day	3,168	16	0.32	0.10	—
	8th day	3,184	36	0.72	0.23	0
	9th day	3,912	40	0.80	0.27	—
	10th day	3,360	24	0.48	0.15	0
	11th day	3,328	32	0.64	0.20	0
	12th day	3,392	32	0.64	0.20	—
20	133286					
	1st day	3,728	16	0.32	0.08	0
	2d day	3,584	56	1.12	0.31	—
	3d day	3,344	48	0.96	0.29	0
	4th day	3,200	40	0.80	0.22	0
	5th day	3,280	80	1.60	0.49	0
	6th day	3,376	32	0.64	0.19	0
	7th day	3,360	112	2.24	0.68	0
	8th day	3,328	64	1.28	0.30	0
	9th day	3,408	96	1.92	0.57	0
	10th day	3,456	64	1.28	0.37	0
	11th day	3,424	40	0.80	0.24	0
	12th day	3,504	32	0.64	0.18	—
21†	133325					
	1st day	3,856	16	0.32	0.09	—
	2d day	3,760	32	0.64	0.14	—
	3d day	3,680	48	0.96	0.27	—
	4th day	3,648	48	0.96	0.27	±
	5th day	3,664	32	0.64	0.18	—
	6th day	3,680	80	1.60	0.41	—
	7th day	3,712	128	2.56	0.69	+
	8th day	3,744	64	1.28	0.35	0
	9th day	3,744	48	0.96	0.26	0
	10th day	3,744	32	0.64	0.17	0
	11th day	3,840	16	0.32	0.09	—
22	133462					
	1st day	3,232	8	0.16	0.05	—
	2d day	3,200	56	1.12	0.35	—
	3d day	3,040	48	0.96	0.32	—
	4th day	2,944	48	0.96	0.33	0
	5th day	2,976	56	1.12	0.39	—
	6th day	3,024	36	0.72	0.24	0
	7th day	3,088	72	1.44	0.46	0
	8th day	3,120	48	0.96	0.31	0
	9th day	3,104	32	0.64	0.21	—
	10th day	3,120	16	0.32	0.10	—
	11th day	3,136	32	0.64	0.21	—
23	133517					
	1st day	4,544	32	0.64	0.14	—
	2d day	4,256	80	1.60	0.38	—
	3d day	4,096	80	1.60	0.39	—
	4th day	4,032	40	0.80	0.20	—
	5th day	4,160	64	1.28	0.31	0
	6th day	4,192	44	0.88	0.21	0
	7th day	4,272	72	1.44	0.34	—
	8th day	4,312	96	1.92	0.45	—
	9th day	4,336	64	1.28	0.30	—
	10th day	4,384	48	0.96	0.22	—
	11th day	4,336	32	0.64	0.15	—

* Pyelocystitis. † Birth injury.

Instead of these children being given plain water between nursings, they were given this weak egg albumin solution, and the quantity of the water thus taken by the infant recorded by the nurse. The precipitin reactions were carried out as mentioned in a previous investigation [9] using an antieggwhite rabbit serum of at least 50,000.

As shown in Table 1, 136 specimens of urine were examined. These were taken from twenty-three different infants. Thirty-three specimens, or 24.3 per cent., gave a positive reaction, but of these eighteen, or approximately 75 per cent., had at one time or another shown one or more positive reactions.

TABLE 2.—DISTRIBUTION OF REACTIONS

Day of Life	Number of Specimens	Positive
1	8	0
2	8	0
3	6	0
4	10	3
5	17	7
6	14	5
7	18	5
8	15	4
9	12	4
10	12	3
11	5	2
12	4	0
13	2	0

TABLE 3.—RESULTS OF EXAMINATION OF CONTROLS

Day of Life	Number of Specimens	Day of Life	Number of Specimens
2	4	8	4
3	3	9	2
4	2	10	4
5	6	11	1
6	3	12	1
7	4		

The first positive reactions were found in the urine obtained on the fourth day of life. The period from the fourth to the eleventh day showed approximately the same proportion of positive reactions for each day. No reactions were obtained after the eleventh day but the number of cases was so small as to take away any significance which might otherwise be attached to this statement.

At no time did the amount of albumin per kilogram for twenty-four hours exceed 0.82 gm. Of the positive reactions the lowest was obtained when the infant received 0.14 gm. per kilogram; and the highest at 0.75 gm.

For controls, forty-one specimens were obtained from seventeen different patients. In no instance was a positive reaction obtained (Table 3).

9. Hektoen and Grulee: Am. J. Dis. Child. **18**:1 (July) 1919.

An observation which may be of some interest is that in six of the cases, sixteen stools had been examined for egg precipitin reaction (these were cases reported in a former paper).[10] In no instance was there a negative reaction in the stool with a positive reaction in the urine. In one case the stool was positive but the urine was negative.

From these examinations it would seem fair to conclude that the intestinal wall of the new-born infant from the fourth to the tenth day, inclusive, is permeable to small quantities of egg white which can be determined by the precipitin reaction in the urine. With these findings it would seem likely that this is not a reaction of specific cases but is a general characteristic of that period of life. The results suggest an explanation of sensitization to egg and other foreign albumin.

We wish to express our thanks to Dr. Ludvig Hektoen of the John McCormick Memorial Institute for supervising the precipitin reactions.

10. Grulee: Am. J. Dis. Child. **20**:15 (July) 1920.

BLOOD VOLUME IN INFANTS ESTIMATED BY THE VITAL DYE METHOD*

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This report is part of a study which is now being carried on in the pediatric department on the problem of the anemias of infancy and childhood. Many studies have been made in this field but most of the work so far done has reference mainly to the blood picture, studies relating to the differential count of the white blood cells, the study of the red blood cells, their number and fragility and to the percentage of hemoglobin; in many instances the postmortem findings are added to these studies of the cells and hemoglobin. All these studies are valuable and have their place in the problem of the anemias but so far they have led to little more than an unsatisfactory classification of the anemias. Even as regards classification there is much confusion and very little has been ascertained as to the etiology of the various anemias which occur so frequently during infancy and childhood. Today we can do little more than divide anemias into primary and secondary groups. We know little as to the specific causes of these anemias. We know the end results well but what has brought about these results we know little of and it would seem that we are likely not to go much further in our understanding of these blood conditions unless we attack the problem from a somewhat different standpoint.

During the past few years a great deal of experimental work has been done on blood, regarding it as an organ. Blood regeneration following certain measures used to injure or modify the functioning of the bone marrow and spleen, as certain bacterial toxins, certain chemical poisons as benzol and saponin or the administration of over exposure to roentgen-ray and radium, have been studied carefully.[1] These investigations have thrown a good deal of additional light on many of the functions of the blood and blood forming organs. The rate of regeneration of the red blood cells is fairly definitely known. The capacity to regenerate following certain of these procedures has also been carefully investigated and we have data now of considerable importance on these points.

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1. Whipple, et al: Series of articles on Blood Regeneration Following Simple Anemias, Am. J. Physiol. **52**:151, 167, 206, 236, 263, 1920.

The many studies on coagulation have differentiated the various factors which enter into this complex function. From the results of these studies we are now able to group various types of hemorrhagic conditions, according to which factor, salt, prothrombin, platelets, fibrinogen, antithrombin, is disturbed. By these means our understanding of these puzzling conditions has been greatly clarified and our measures for combating or favorably effecting them has been materially advanced.[2] The close relationship of some of these hemorrhagic conditions, such as purpura hemorrhagica, to the group of the little understood primary anemias, aplastic anemias, has been pointed out by Minot.[3]

Equally important are the studies on pigment production and destruction in the blood for a better understanding of the functions of blood considered as an organ. The part the liver plays on this pigment formation has been carefully worked out by Whipple and his associates[4] in their anemia studies on bile and plood pigment. They have pointed out the part the liver plays in pigment formation. So far, clinically, little or no attention has been paid to hemoglobin beyond the estimation of the percentage of hemoglobin found in various blood disturbances. Unfortunately, most of the numerous reports are based on inaccurate methods of estimating hemoglobin and this notwithstanding the fact that Van Slyke,[5] and Palmer[6] and more recently Robscheit[7] have pointed out the inaccuracies of older methods and the latter has described a simple accurate adaptation of their methods for clinical use.[7] They have shown that the estimation of hemoglobin by the Tallqvist methods and others now in common clinical use have an inaccuracy of from 15 to 30 per cent. which in some cases runs as high as 50 per cent. from a correct estimation of hemoglobin as done by the Palmer modification.

Before one can even begin to make a study of the anemias there are certain questions that must be definitely answered, questions for which we have at present no normal standards. It is first necessary to obtain figures on which to base our studies. We have been fortunately placed for making these studies on anemias of infancy and childhood because for the past three years researches on these problems have been in progress and are now in progress at the Hooper Foundation for Medical Research.

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2. Hurwitz, S. H., and Lucas, W. P.: A Study of the Blood in Hemophilia, Arch. Int. Med. **17**:543 (April) 1916.
3. Minot, G. R.: Arch. Int. Med. **19**:1062 (June) 1917.
4. See Ref. 1.
5. Van Slyke, D.: J. Biol. Chem. **33**:127, 1918.
6. Palmer: J. Biol. Chem. **41**:209, 1920.
7. Robscheit, F. S.: J. Biol. Chem. **41**:209, 1920.

One of the first of these questions to be settled is that of a normal blood volume in infancy and childhood. It is needless to point out that we cannot go very far in any comprehensive understanding of the blood as an organ without some idea as to the volume of blood normally in circulation, its normal variations at different periods and under varying conditions of nutrition and growth. The first point we have attempted to arrive at any conclusion on is the normal blood volume in infancy. This paper deals mainly with the normal variations during the first year. We have only a few examples of blood volumes in infants suffering from some form of secondary anemia.

HISTORICAL

Keith, Rowntree and Geraghty [8] first used the dye method for estimating the blood volume. In their studies they used vital red and demonstrated that the normal blood volume for adults is about 8.8 per cent. or 1-11.4 of the body weight. Unfortunately, their supply of dye was limited and on account of the war they were unable to procure more to carry on their studies.

For several years Dr. Herbert M. Evans has been studying the various dyes in his investigations on vital tissue staining. From his work he was able to suggest that brilliant vital red would most probably be the dye best suited for blood volume studies. Dr. Whipple and his associates have tested this dye out in many hundreds of experiments and have found that it answers the requirements for a satisfactory dye. First, because it is nontoxic when injected intravenously, even in large doses fifteen times that used in the estimation of plasma volume. Second, this dye is not taken up by any of the red blood cells or tissues but remains for a comparatively long time in the plasma but the ultimate fate of the dye is not known. Third, it can easily and accurately be determined by colorimetric methods. The use of this dye in dogs has shown that the normal healthy growing dog has an average blood volume of 10.1 per cent. body weight. So far as we know this method has not been applied to infants or children. During early infancy this method can be easily carried out by using the longitudinal sinus, and thanks to the Goldbloom [9] block we have a safe device for the accurate injection of dye. Without this block the work would have been much more difficult, in fact we started some of these studies before we were able to secure this simple device and we can testify that it has facilitated our work and made us feel far more confident in persisting with the repeated injections of the dye on so many cases. In working with new-born infants this block is indispensable. The sinus was used by us in all

8. Keith, Rowntree and Geraghty: Arch. Int. Med. **16**:547 (Sept.) 1915.
9. Goldbloom, A.: Am. J. Dis. Child. **16**:388 (Sept.) 1918.

our studies, except the few we have done in children over 18 months old. In these older children we have used either the jugular veins or the veins at the elbow, the latter where they are large enough, we have found easier to work with than the jugular veins, for as will be seen there is a certain minimum of manipulation necessary in changing syringes which makes it difficult to use the neck veins.

PROCEDURE

Ten c.c. of blood are withdrawn into a Record syringe which has been sterilized and thoroughly washed out with sterile salt solution. This first sample of blood is immediately discharged into an accurately calibrated 15 c.c. centrifuge tube (hematocrit tube) which contains 2 c.c. of a 1.6 per cent. solution of sodium oxalate;[7] the blood and oxalate are thoroughly mixed by inverting the tube several times so as to obviate any possible clotting. The centrifuge tube is then stoppered. From this tube the hematocrit readings are made and the serum for making the standard control dye mixture is taken. Before this first sample of blood is taken the standard amount of dye solution is drawn up into a Record syringe along with enough physiologic sodium chlorid (0.9) solution to make sure that all the dye has been taken up into the syringe from the small containing dish in which the measured amount of dye is placed.

The dye solution is a 1.5 per cent. solution and is given in the amount of 1 c.c. per 5 kg. of body weight, which gives 3 mg. of the dye per kilogram. The dye solution is injected into the sinus, immediately after the first 10 c.c. of blood have been withdrawn, using the same needle, only changing the syringe, the dye being completely washed out by drawing blood back and forth several times into the syringe after the dye has been emptied out of the syringe into the sinus. We have found this the most convenient and satisfactory way of being sure that all the dye had been delivered into the sinus. We have had no untoward happenings while following this method. The needle is then withdrawn; exactly four minutes after the injection of this dye a clean needle is again inserted into the sinus and a sample of 16 c.c. of blood is withdrawn and discharged immediately into two petrolatum lined test tubes about equally distributed. This furnishes the plasma for the estimation of the blood plasma volume. All the tubes are now placed in the ice chest for at least half an hour, then centrifuged at 2,500 revolutions a minute for half an hour. In the hematocrit tube, (accurately calibrated centrifuge tube) the total amount of fluid is noted and the number of cubic centimeters of blood cells, red and white, are noted. This gives the total hematocrit reading when 2 c.c. is subtracted for the oxalate dilution and the hematocrit reading for the red blood cells. Five c.c. of this serum

are pipetted off and to this is added 5 c.c. of a 0.9 per cent. sodium chlorid solution and 5 c.c. aqueous dye solution. This dye solution is made up as follows: 0.5 c.c. of a 1.5 per cent. brilliant vital red is pipetted into a 100 c.c. volumetric flask which is then filled up to the mark with distilled water. This gives the standard against which is read the unknown dye colored plasma. The dye colored serum is pipetted off from the petrolatumed tube and 2 c.c. of this serum is diluted with 4 c.c. of a 0.9 per cent. sodium chlorid solution, which gives the same dilution to this serum as the standard dye solution made from patient's dye free plasma, to which has been added a known amount of dye and salt solution.

After mixing thoroughly, the standard dye-plasma solution and serum solution are allowed to stand for fifteen minutes, so that the intensity of color may be uniform. The standard dye solution is then put into the colorimetric wedge (we have used in all our work the Hellige colorimeter and have found it perfectly satisfactory. It has been tested against the Duboscq and found accurate) and each of the samples of the unknown serum dye solution is read against this. The average of three readings is taken as the color percentage of the sample.

COMPUTATION RESULTS

From the hematocrit readings the plasma per cent. and the red cell per cent. may easily be calculated—the red cell hematocrit reading is read from the hematocrit tube, taking the total hematocrit reading minus 2 and the plasma hematocrit reading by subtracting the total cell hematocrit reading from the total hematocrit reading minus 2.

$$\text{Plasma volume in c.c.} = \frac{\text{Weight in kilograms} \times 40}{\text{Average colorimetric reading}} \times 100$$

$$\text{Blood volume in c.c.} = \frac{\text{Plasma volume}}{\text{Plasma per cent.}} \times 100$$

The plasma per cent. means the per cent. of the whole blood which the plasma constitutes and is obtained by dividing the total number of cubic centimeters of oxalated plasma present in the hematocrit tube minus 2 by the total contents of the tube in cubic centimeters minus 2. The red cell per cent. is calculated from the hematocrit tube by dividing the red cell reading by the total hematocrit reading minus 2. The blood volume is divided by the body weight in kilograms which gives the blood volume in c.c. per kilograms of body weight and the percentage of blood to body weight is derived from this figure by simply pointing off one place. The pigment volume is obtained by multiplying the hemoglobin per cent. by the blood volume. This gives a valuable index of the curve of blood regeneration.

TABLE I.—CHART A. OF THIRTY NEW-BORN INFANTS' BLOOD VOLUME ESTIMATIONS FROM TWO AND ONE-HALF HOURS TO FIFTEEN DAYS. IN MOST CASES ONLY SINGLE COMPUTATIONS FOR EACH CASE WERE MADE

No.	Age	Sex*	Birth Weight	Weight Day of Blood Volume	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume C.c.	Blood Volume, C.c.	Blood per Kg. C.c.	Pigment Volume	Hb., per Cent.	Red Blood Cells	Weight Day Following Blood Volume	Disc. Weight 14th Day	Reaction	Length at Birth, Cm.	Remarks
6830	30 hrs.	♂	3,560	3,495	11.3	28.0	70.5	152	542	155	672	124	6,480,000	3,330	3,680	None	52	
6639	12 hrs.	♂	3,915	3,860	11.3	48.5	49.5	214	441	114	432	98	5,640,000	3,700	3,615	None	53	
6771	28 hrs.	♀	2,900	2,830	12.5	38.4	61.5	169	441	157	467	106	7,200,000	2,790	3,250	T 37.4	50	
6771	15 days	♀	2,900	3,270	11.3	53.0	46.0	247	465	142	348	75	.....	3,250	3,250	None T 38.5	50	
6619	11 days	♀	2,650	2,550	11.2	50.0	49.1	170	340	133	306	90	4,290,000	2,550	2,610	Drowsy	49	3 minutes late, obtained dyed blood
6786	5 hrs.	♀	3,370	3,370	11.4	34.2	63.0	184	540	160	615	114	4,730,000	3,430	3,765	None	51	
6723	8 hrs.	♀	2,710	2,710	8.1	41.3	56.5	193	469	173	483	103	.....	2,510	2,675	None	50	
6820	48 hrs.	♀	3,745	3,560	12.2	44.7	54.0	264	590	165	601	102	5,080,000	3,580	3,625	Vomited dur. B. V.	52	
6785	32 hrs.	♂	3,710	3,620	11.3	42.0	57.0	263	627	173	664	106	5,050,000	3,625	4,080	None	53	
6816	24 hrs.	♀	3,390	3,470	12.2	37.3	61.4	252	676	195	770	114	.....	3,535	3,790	T 37.8	52	
6628	9 days	♂	3,080	2,890	10.7	41.5	57.5	154	372	129	405	109	4,660,000	2,845	2,935	None	49	
1482	3 days	♂	3,220	3,150	9.8	42.9	56.0	156	364	116	382	105	5,644,000	3,170	3,410	None	50	
6904	3 days	♀	3,150	3,060	10.75	46.5	52.0	177	382	125	...	...	.....	2,960	3,325	None	50	
6090	4 days	♂	3,420	3,410	12.0	46.3	52.5	204	440	125	...	...	.....	3,320	3,550	None	53	
6712	10 hrs.	♀	3,010	2,890	12.4	45.5	53.6	160	354	122	354	100	5,060,000	.....	.....	.....	50	Died jaundiced
6622	4 days	♂	3,850	3,740	10.5	36.7	62.3	199	545	146	588	108	5,992,000	3,700	3,765	None	52	
6310	5 days	♀	2,980	2,980	12.0	42.5	56.75	192	454	152	444	98	.....	2,960	3,190	None	51	
6670	6 days	♂	3,400	3,300	11.8	42.8	56.0	209	490	149	534	109	5,420,000	3,240	3,515	None	50	
6812	15 hrs.	♂	3,275	3,275	11.75	37.8	59.5	136	361	110	393	109	5,140,000	3,200	3,310	None	51	2 minutes late, obtained dyed blood
6801	2½ hrs.	♀	3,350	3,350	8.6	36.0	61.6	184	513	155	523	102	.....	3,120	3,080	None	50	
6948	14 hrs.	♀	4,465	4,460	12.25	33.0	65.3	283	857	192	899	105	.....	4,390	4,280	None	53	2 minutes late
Schn.	36 hrs.	♀	3,320	3,160	10.3	40.0	58.0	204	507	161	496	98	.....	3,200	.....	None	52	
Flax.	32 hrs.	♀	3,030	2,950	10.6	41.5	57.0	137	331	112	307	93	4,648,000	3,010	.....	T 37.4	49	
Turt.	26 hrs.	♀	3,325	3,230	8.8	37.5	61.5	142	378	117	359	95	.....	3,290	.....	None	49	
Kan.	3 hrs.	♀	2,980	2,980	11.5	35.7	53.4	159	446	150	...	...	.....	2,850	.....	None	51	
2743	6 hrs.	♂	4,130	4,130	11.75	31.0	67.0	202	595	144	702	118	5,696,000	.....	.....	None	56	
Tiff.	12 hrs.	♀	3,845	3,720	11.2	43.7	55.3	245	566	153	549	97	5,552,000	3,720	.....	Cyanotic drg. test	54	2 minutes late, obtained dyed blood
Carl.	49 hrs.	♂	2,800	2,950	10.5	35.7	62.8	227	635	188	857	135	5,520,000	2,950	.....	None	49	
Kado.	24 hrs.	♂	2,880	2,880	10.25	30.7	67.2	170	553	192	635	115	5,464,000	2,975	.....	None	50	
Kayr.	17 hrs.	♂	3,550	3,390	10.8	51.9	46.3	188	363	107	304	84	.....	3,310	.....	None	51	3 minutes late

* In this column, ♂ signifies male, and ♀ female.

TABLE 2.—Chart B: Of Thirty Newborn Infants, Blood Volume Estimations From Two and One-Half Hours to Fifteen Days. Grouped According to Age

Age	Weight in Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Gain or Loss Before Blood Volume
3 hrs.	3,350	8.6	36.0	61.6	184	513	155	None
3 hrs.	2,980	11.5	35.7	63.4	159	446	150	None
5 hrs.	3,370	11.4	34.2	63.0	184	540	160	None
6 hrs.	4,130	11.75	31.0	67.0	202	595	144	None
8 hrs.	2,710	8.1	41.3	56.5	193	469	173	None
10 hrs.	2,890	12.4	45.5	53.6	160	354	122	None
12 hrs.	3,720	11.2	43.7	55.3	245	566	153	—120 G
12 hrs.	3,860	11.3	48.5	49.5	214	441	114	— 55 G
14 hrs.	4,460	12.25	33.0	65.3	283	857	192	None
15 hrs.	3,275	11.75	37.8	59.5	136	361	110	None
24 hrs.	3,470	12.2	37.3	61.4	252	676	195	—120 G
24 hrs.	2,880	10.25	30.7	67.2	170	553	192	—165 G
26 hrs.	3,230	8.8	37.5	61.5	142	378	117	— 95 G
28 hrs.	2,830	12.5	38.4	60.0	169	441	157	— 70 G
30 hrs.	3,495	11.3	28.0	70.5	152	542	155	— 65 G
32 hrs.	2,950	10.6	41.5	57.0	137	331	112	— 80 G
32 hrs.	3,620	11.3	42.0	57.0	263	627	173	— 90 G
36 hrs.	3,160	10.3	40.0	58.0	204	507	161	—160 G
48 hrs.	3,560	12.2	44.7	54.0	264	590	165	—185 G
49 hrs.	2,950	10.5	35.7	62.8	227	635	188	+150 G
3 days	3,060	10.75	46.5	52.0	177	382	125	— 90 G
3 days	3,150	9.8	42.9	56.0	156	364	116	— 70 G
4 days	3,740	10.5	36.7	62.3	199	545	146	—110 G
4 days	3,410	12.0	46.3	52.5	204	440	128	— 10 G
5 days	2,980	12.0	42.5	57.0	192	454	152	None
6 days	3,300	11.8	42.8	56.0	209	490	149	—100 G
9 days	2,890	10.7	41.5	57.5	154	372	129	—190 G
11 days	2,550	11.2	50.0	49.1	170	340	133	—100 G
15 days	3,270	11.3	53.0	46.0	247	465	142	+370 G
15 days	2,930	9.8	49.0	49.5	167	342	117	

TABLE 3.—Chart C: Of Thirty New-Born Infants, Blood Volume Estimations From Two and One-Half Hours to Fifteen Days. Grouped According to Weight

Weight in Gm.	Age	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	C.c.	Blood per Kg., C.c.	Pigment Volume	Hb.	Red Blood Cells	Weight Loss or Gain Before Blood Volume
2,550	11 days	11.2	50.0	49.1	170	340	133	306	90	4,290,000	—100 G
2,710	8 hrs.	8.1	41.3	56.5	193	469	173	483	103	.....	0
2,830	28 hrs.	12.5	38.4	61.5	169	441	157	467	106	7,200,000	— 70 G
2,880	24 hrs.	10.25	30.7	67.2	170	553	192	635	115	5,464,000	
2,890	10 hrs.	12.4	45.5	53.6	160	354	122	354	100	5,060,000	—120 G
2,890	9 days	10.7	41.5	57.5	154	372	129	405	109	4,660,000	—190 G
2,950	32 hrs.	10.6	41.5	57.0	137	331	112	307	93	4,648,000	— 80 G
2,950	49 hrs.	10.5	35.7	62.8	227	635	188	857	135	5,520,000	+150 G
2,980	3 hrs.	11.5	35.7	63.4	159	446	150				
2,980	5 days	12.0	42.5	56.75	192	454	152	444	98		
3,060	3 days	10.75	46.5	52.0	177	382	125	...	...	.....	— 90 G
3,150	3 days	9.8	42.9	56.0	156	364	116	382	105	5,644,000	— 70 G
3,160	36 hrs.	10.3	40.0	58.0	204	507	161	496	98	.....	—160 G
3,230	26 hrs.	8.8	37.5	61.5	142	378	117	350	95	.....	— 95 G
3,270	15 days	11.3	53.0	46.0	247	465	142	348	75	.....	+370 G
3,275	15 hrs.	11.75	37.8	59.5	136	361	110	398	109	5,140,000	
3,300	6 days	11.8	42.8	56.0	209	490	149	534	109	5,420,000	—100 G
3,350	2½ hrs.	8.6	36.0	61.6	184	513	155	523	102		
3,370	5 hrs.	11.4	34.2	63.0	184	540	160	615	114	5,730,000	
3,390	17 hrs.	10.8	51.9	46.3	188	363	107	304	84		
3,410	4 days	12.0	46.3	52.5	204	440	125	...	...	.....	— 10 G
3,470	24 hrs.	12.2	37.3	61.4	252	676	195	770	114	.....	—120 G
3,495	30 hrs.	11.3	28.0	70.5	152	542	155	672	124	6,480,000	— 65 G
3,560	48 hrs.	12.2	44.7	54.0	264	590	165	601	102	5,080,000	—185 G
3,620	32 hrs.	11.3	42.0	57.0	263	627	173	604	106	5,050,000	— 90 G
3,720	12 hrs.	11.2	43.7	55.3	245	566	153	549	97	5,552,000	—125 G
3,740	4 days	10.5	36.7	62.3	199	545	146	588	108	5,992,000	—110 G
3,860	12 hrs.	11.3	48.5	49.5	214	441	114	432	98	5,640,000	— 55 G
4,130	6 hrs.	11.75	31.0	67.0	202	595	144	702	118	5,696,000	
4,460	14 hrs.	12.25	33.0	65.3	283	857	192	899	105	.....	—170 G

DISCUSSION

It is interesting to note the great variation of blood volume per cent. in new-born infants, which ranges from 10.7 to 19.5 per cent. of body weight and from 107 to 195 c.c. per kilogram and the pigment volume from 304 to 899 c.c. The averages for these are: blood volume per cent., 14.7; blood volume per kilogram, 147 cc.; and pigment volume 521 c.c. Another one of the interesting variations is that found between plasma volume and red cell volume. The plasma volume per cent. is small as compared with the relatively high red cell percentage. These findings are fairly constant in the new-born during the first ten days. We can ascribe no reason for these wide variations beyond the fact that the blood during the first few days is undergoing a definite adjustment to its new surroundings. We know from studies on blood proteins and blood sugars, that a similar wide variation occurs during these first few days before the normal averages are established and the blood volume undoubtedly goes through this same period of adjustment when the blood forming organs are probably called on to function independent of any assistance from the maternal circulation. Of course it is not assumed that the blood forming organs have not been functioning throughout the fetal period but certainly during the first few days there must be some very definite adjustment to be established and it is therefore not surprising to find wide individual variations with rapid changes in accommodation taking place. We all know how easily blood changes occur during this period and how difficult it is for them to right themselves when any factor intervenes to disturb in any way the blood forming organs. There does not seem to be any constant correlation between blood volume and either weight, length or age in hours or days up to fifteen days.

In the infants tested who were from 15 days to 1 year of age, there is a very definite uniformity, constant at least for individuals and the variations between individuals are very much less marked than in the first fifteen days, the extremes being from 9.0 to 12.6 per cent. and the average 10.9 per cent. There seems to be a fairly definite attempt to stabilize the blood volume during the first few months and for any given infant over a period of several months at least the blood volume apparently remains at a fairly constant level as is shown in Table 4, except where some condition has intervened which might easily be assumed to have changed the blood volume.

In the pathologic cases changes from the normal blood volume are quite striking. We do not desire to discuss these variations at this time but hope to enlarge our number of studies in time in order to be able to form a more definite idea as to the factors which effect

TABLE 4.—Eleven Fairly Normal Infants, Aged From Fifteen Days to One Year

Name	Diagnosis	Age	Weight, Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Hb., per Cent.	Pigment Volume	Reaction
B. O.	Normal	15 days	2,930	9.8	49.0	49.5	167	342	117	..	...	Temp. 38 C. then immediately normal, otherwise O.K.
	Normal	39 days	3,350	10.7	65.4	33.6	257	393	117+	63	247	Slight loss, O.K.
		50 days	3,560	10.8	67.5	31.5	279	413	116	52	214	No reaction
B. H.	Normal	4 mos.	5,070	9.0	61.2	37.8	357	582	115	61	354	No reaction
	Normal	4½ mos.	5,270	10.9	60.5	38.1	364	601	114	60	360	Temp. 38.4 C.,otherwise O.K.
		5 mos.	5,190	10.0	63.5	33.5	384	605	117	50	302	No reaction
		5½ mos.	5,560	10.4	65.5	33.6	420	640	115	..	...	No reaction
B. R. H.	Normal	9½ mos.	7,260	9.2	63.1	35.8	519	822	113	60	493	Temp. 39.4 C., loss 90 gm., O.K.
	Normal	10 mos.	7,470	12.3	65.8	33.3	543	825	110	52	428	Temp. 38 C., loss 30 gm., O.K.
B. S.	Hare-lip	4 mos.	4,940	11.7	65.75	32.5	387	589	119+	..	...	No reaction
	Cleft palate	4½ mos.	4,910	10.0	65.5	33.5	378	576	117+	..	...	Temp. 39 C., O.K.
		6 mos.	6,290	10.75	62.0	36.8	426	687	109+	59	405	No reaction
B. T.	Feeding case	10 mos.	6,120	8.5	62.4	37.0	371	595	97	..	...	No reaction
	Rickets	10¼ mos.	6,250	11.6	64.7	34.4	374	577	92	..	...	Temp. 39.2 C., vomited 9 times, O.K.
			6,300	9.8	68.4	30.6	400	585	93	..	...	No reaction
B. J.	Normal	2½ mos.	3,760	12.05	65.0	34.1	239	367	97	..	...	No reaction
	Normal	3 mos.	3,920	9.5	72.5	26.3	275	380	97	..	...	No reaction
B. V.	Spasmophilia	7 mos.	5,350	9.0	64.0	35.0	362	566	106	..	...	Loss 140 gm., O.K.
	Rickets	7½ mos.	5,600	10.55	66.0	33.2	361	546	97	..	...	Loss 40 gm., O.K.
B. B.	Eczema	11½ mos.	6,510	9.9	58.0	40.9	473	815	126	62	505	No reaction
		12 mos.	6,420	10.5	60.9	38.0+	494	811	126	57	462	Temp. 38 C., otherwise negative
B. L.	Hydrocephalus	7 mos.	4,650	10.9	62.8	36.2	339	538	116	..	...	13 minutes late; no reaction
		7½ mos.	4,710	11.0	62.4	36.8	363	581	123	..	...	No reaction
		8 mos.	5,000	10.6	63.6	35.9	364	572	114	..	...	Loss 50 gm., O.K.
B. W.	Feeding case	6 mos.	4,170	10.2	66.0	33.8	300	468	112	52	243	No reaction
		6½ mos.	4,320	11.0	66.0+	32.2	339	509	117	55	279	No reaction
B. N. B.	Birth palsy	10 mos.	7,800	12.2	65.5	34.0	465	710	91	..	...	No reaction
		10¼ mos.	7,900	9.75	65.1	33.8	466	714	90.3	..	...	No reaction
		11 mos.	7,980	9.1	67.5	31.3	614	908	114	..	...	Temp. 38.4 C., otherwise O.K.
		11¼ mos.	8,180	10.9	68.7	30.3	617	900	110	..	...	Temp. 40 C., otherwise O.K.

TABLE 5.—Of Three Infants With Fairly Marked Secondary Anemia

Name	Diagnosis	Age	Weight, Gm.	Total Hemat., C.c.	Plasma, per Cent.	Red Cell, per Cent.	Plasma Volume, C.c.	Blood Volume, C.c.	Blood per Kg., C.c.	Hb., per Cent.	Pigment Volume	Reaction
B. K.	Premature.....	12 mos.	6,420	11.0	75.0	24.0	378	504	78.5	..	...	No reaction
		12¼ mos.	6,520	10.6	77.0	22.7	373	485	74.5	25	121	Temp. 39.2 C., loss 70 gm.
		12½ mos.	6,780	9.5	79.5	20.0	418	525	77.5	25	131	Temp. 38.2 C., otherwise O.K.
B. F.	Premature.....	5½ mos.	3,080	10.9	72.0	27.0	216	300	97.5	52	156	Temp. 38.6 C.
		5¾ mos.	3,210	9.6	76.5	22.9	225	294	92.0	52	153	None
		6 mos.	3,280	10.2	80.2	18.6	230	288	87.5	..	...	Refused feedings for 2 days
B. C.	Premature.....	7½ mos.	3,550	11.9	73.1	26.0	233	318	89.9	45	143	Temp. 39.6 C.
		8¼ mos.	3,830	10.5	80.5	19.0	295	366	95.6	25	91.5	None; loss 60 gm.
		8½ mos.	3,860	10.55	82.5	17.0	351	425	110.0	20	85	Temp. 38.2 C. (otitis media)
		9 mos.	4,760	10.1	69.2	29.0	390	560	118.0	37	207	No reaction

or produce these variations. Some points are, however, interesting enough to be emphasized. In B. K. (Table 5) the blood volume is very low, from 74.5 to 78.5 c.c. per kilogram of body weight. He was a typical fat, water-logged baby of the type so often seen which has been fed on a high carbohydrate diet. His plasma per cent., from 75 to 79.5, was very high in comparison with the other normal children of his age as B. N. B. who had a blood plasma of from 65 to 68.7 per cent. and a blood volume of from 90.3 to 114 c.c. per kilogram. B. F. and B. C. show the blood volume of quite marked secondary anemia so often found in premature infants. B. C., in addition, has as marked a clinical type of rickets as is often seen. Their plasma per cent. was also very high (from 69.2 to 82.5) and their red cell per cent. from 17 to 29, very low, as might be expected. In another case of severe anemia in an older child, not here reported, the plasma volume ran up to 85+ per cent. and the red cell percentage was 14.

While making these studies on blood volume, we have been struck by the practically uniform appearance of bile pigment in the serum of the new-born infants. The serum when pipetted off has a yellowish color. We have had several samples tested for bile pigment and in all bile pigments have been demonstrated.

Bang [10] found bile pigment in the blood obtained from the umbilical cord. He concludes that icterus in the new-born is a physiologic condition and the amount of pigment shows a constant increase in the blood after the first few days; he considers it only a question of degree between the new-born with or without icterus neonatorum. Our findings would corroborate Bang's findings. In many of our cases icterus, in so far as we were able to observe it, never appeared.

We are now making a more careful analytical study of this condition and hope to report on it in the near future. This undoubtedly has a distinct bearing on the appearance of certain of the hemorrhagic conditions of the new-born. In one of our babies which showed icterus almost from birth (it was observed when 4 hours old) bile pigment was present in very large amounts as shown by the marked discoloration of the serum when we made our blood volume determinations at 10 hours of age.

Thanks are due Dr. Whipple and Mrs. Robscheit for their many suggestions and valuable assistance on this report and on our further studies which are in progress.

We wish to thank Mr. Francis Smyth of the Hooper Foundation for Medical Research, who tested the samples for bile pigments, using the method described by Hooper and Whipple.[11]

10. Bang, F.: Jaundice of the Newly-Born, Hospitalstidende **8**:637 (June) 1915.

11. Hooper and Whipple: Am. J. Physiol. **40**:332, 349 (April) 1916.